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# *TRICHOMONAS VAGINALIS* IN PREGNANCY THE RESULTS OF METRONIDAZOLE THERAPY ON THE MOTHER AND CHILD

BY

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ONE hundred and twenty-five years ago Donné (1836) the French investigator, first described the *Trichomonas vaginalis*. Hoehne (1916) eighty years later adopted the view that *Trichomonas vaginalis* was an aetiological factor in vaginitis. Little progress, when compared with other organisms, has been made in its biological, biochemical and epidemiological history. Recent conventions in Paris, Montreal and London have contributed to a more widespread knowledge of the organism and its clinical significance. Improved cultural techniques have aided human and animal experimentation. It has been proved that the organism remains viable outside the host over longer periods than were previously considered possible. Burch and his colleagues (1959) cultured the organism from damp infected towels up to twenty-five hours. Whittington (1957) cultured the protozoa from infected bakelite lavatory seats after forty-five minutes at room temperature.

The pathogenicity of the organism is still debatable. Many investigators regard it as non-pathogenic, in view of its recovery from normal vaginas in asymptomatic cases, pathogenicity developing under certain conditions. Moore and Simpson (1954) regarded emotional upsets of great importance. Other suggested factors are intercurrent infections, hormonal changes and trauma either from the use of contraceptives or sexual intercourse. Spontaneous clinical cures are known to occur.

## INCIDENCE IN PREGNANCY

Most investigators agree that the incidence of infection is higher in the pregnant than the non-pregnant woman. Trussell (1947) found 28·9 per cent of 433 pregnant women infected, compared with 17·9 per cent of 703 non-pregnant cases. In pregnancy the higher incidence is probably due to: discontinuation of contraceptives, many of which are trichomonacidal (Whittington, 1951), a tendency for more frequent sexual intercourse in the early months of pregnancy (especially amongst prostitutes), local hormonal changes and the emotional upsets in unwanted pregnancies. The trichomonas has not in the past been considered as a cause of abortion. However, studies of aborted women and the products of abortion might prove interesting. The trichomonas-foetus occurring in cattle may cause a balanitis in bulls, and pyometra, abortion and sterility in cows. Although estimated to affect less than 0·5 per cent of cattle, this organism has been demonstrated in the amniotic fluid of the aborted calf.

The protozoa have been reported far more commonly in coloured patients, either pregnant or non-pregnant. This higher incidence may be due to overcrowding, sexual promiscuity and the lack of contraception.

## COMPLICATIONS ASSOCIATED WITH TRICHOMONIASIS OF PREGNANCY

*Psychological*

Many women may develop a fear of venereal disease, or that their pregnancy is not proceeding normally.

*Clinical*

(1) Widespread condylomata acuminata due to a virus may develop as a result of the

hyperaemia and moisture of the trichomonal infection.

(2) A blood-stained discharge may develop due to an acute vaginitis or an acute cervical erosion.

(3) Urethritis and an associated cystitis may be responsible for increased frequency of micturition and lower abdominal discomfort. The protozoa have been demonstrated in the pelvis of the kidney; extension to the renal pelvis would be more prone to occur if a physiological hydro-ureter of pregnancy existed.

(4) Painful urethral carunculosis may accompany the urethritis.

Seitz (1919) and Carretti (1938) suggested that the presence of the trichomonad increased the puerperal morbidity rate. Neumann (1926), Crown (1933) and Trussell *et al.* (1942) have not confirmed this. This infection should however be considered in cases of pyrexia associated with a foul lochial discharge developing three to four weeks after confinement.

## Technique of Diagnosis

*Trichomonas vaginalis* is the only flagellated protozoon known to occur in the vagina. Diagnosis may be made by the immediate examination of wet preparations, by culture or by stained films. Wet preparations are prepared by mixing a little of the vaginal discharge with a small amount of normal saline, and examining under the 1/6 lens. To facilitate recognition of the organism Safranin dye may be added to the normal saline to make an 0·1 per cent final dilution. The discharge is collected from the posterior vaginal fornix and the vaginal mucosa in its vicinity, either by a probe, platinum loop, pipette or spoon. Warming of the slide will enhance motility of the organism if the latter is sluggish. Cultural methods may be employed where facilities for immediate examination are not available, in the transport of specimens to a central laboratory or to confirm doubtful cases. A sterile probe may be dipped in the discharge and put directly into Stuart's carrying media, whence later it will be transferred to the special media, or put immediately into the special media such as Whittington's. The staining of smears is time-consuming and requires a great deal of practice to get good results. The best results are obtained by making a very fine film of diluted discharge on a warm slide, or by fixing the smear with Osmic acid vapour (which is expensive) or by using Meyer's egg albumin. The smear can then be stained later by Leishman's or Giemsa's method.

In female clinics the organism may be demonstrated from the vagina, urethra, Skene's or Bartholin's glands and from urinary sediment after careful centrifuging. Allen and Butler (1946) demonstrated the organism in urine in 21 per cent of 234 cases of female trichomoniasis. Failure to examine extra-vaginal foci is responsible for many clinical relapses. Ideally, all male partners should be examined and treated, in some circumstances empirically. In men the organism may be found in the following sites: the urethra, sub-preputial sac, prostate gland, bladder, and occasionally in the seminal fluid.

## Treatment Past and Present

Local therapy has been the standard treatment in the past. Results were good where the trichomonad was confined to the vagina. Where other foci were involved re-infection of the vagina was common. Many of the preparations formerly used contained Acetarsone, an arsenical derivative. Pregnant women are known to be sensitive to arsenic. It was found that many cases treated by these drugs developed either a local or generalized dermatitis, the latter occasionally simulating German measles. Cases of encephalitis have also been described. Male partners in some instances developed local reactions to the pessaries.

An effective systemic treatment, whereby all foci of infection would benefit, is undoubtedly the answer to the problem. Recently surveys have been conducted in this country and abroad, using the new oral drug Metronidazole. The consensus of opinion is that it is an excellent preparation, although it is not an invariable cure. The majority of the female cases were non-pregnant.

## Chemical Composition of Metronidazole

Metronidazole, now designated Flagyl, is a nitro-derivative of imidazole with a formula of

1-B hydroxyethyl-2 methyl-5 nitroimadazole. It is supplied in tablets containing 200 mg. of metronidazole. As it is a nitroimidazole the drug was given initially to non-pregnant patients. In the labour survey it was found that there was increased absorption of the drug in those patients in whom gastric lavage had been previously carried out before oral treatment was commenced (MG-N, G-N, P-R, R-G). Tablets were given after meals to the pregnant women.

*In vivo* studies of Flagyl on the *Treponema pallidum* were done in the department, in view of the increase of acute infectious syphilis in this country. The drug appears to have no treponemacidal properties.

## Survey

### Part I. Antenatal Series

Flagyl has no contraceptive action. Pregnancies have occurred during the observation periods following upon therapy; in 2 cases of previous sterility conception took place at 6 and 8 weeks respectively after the completion of the course of tablets. Examinations of seminal fluid, conducted in the male department on men receiving therapy, showed normal spermatogenesis.

In all, 65 pregnant women suffering from trichomoniasis have been treated with Flagyl and 16 of these patients have now had normal confinements with healthy babies. One patient had a seven-month baby which lived three days. Death occurred as the result of oesophageal atresia and cerebral haemorrhage. In this case Flagyl was administered for seven days at the fifth month of pregnancy; but it was not considered to be the cause of the congenital condition.

No serious toxic effects have been noted, and no skin eruptions have been encountered. In two cases therapy was discontinued, one because of profuse vomiting, the other because of acute abdominal pain. Both conditions subsided when the drug was stopped. Minor upsets occurred as follows: 5 cases of nausea, 3 of lower abdominal pain (one had loose motions), 2 cases of bitter taste in the mouth, and 3 patients reported with dirty furred tongues. Yeasts were cultured from all affected tongues. Flagyl is secreted in the saliva and it is possible it may precipitate a fungoid condition.

The vaginal flora was graded as recommended by Schroeder.

| Grade | Vaginal Smear | No. of Cases |
|---|---|---|
| I | Lacto-bacilli present | 2 |
| II | Lacto-bacilli and other bacteria | 19 |
| III | Bacteria other than lacto-bacilli | 44 |

*Regime of Survey*

A general medical overhaul was carried out in all cases, including blood tests, urine and blood analyses and followed by a genital examination to exclude any concomitant infection.

Any patient with a past or present history of renal infection, low haemoglobin estimation or a previous history of eclampsia was excluded. Full co-operation of the patient in taking the tablets as advised, and the need for regular attendance were also stressed. Two patients were given 21 Flagyl tablets, one tablet three times daily for seven days. They were re-examined at the end of treatment and whenever possible at 2, 3, 4, 6, 8, 12, 16 and 20 weeks after their initial attendance. In some instances attendances were more frequent because of some other complicating factor. Intercourse was discouraged or the use of a sheath advised. Patients were advised to report back immediately if they developed symptoms of severe nausea, mouth or throat infections or any febrile condition which might suggest an agranulocytosis.

A significant study was only applicable in 40 of the cases, either through default, irregular attendances change of address or transference to other clinics or to their own doctor's care.

In the survey of the 40 patients, 8 were found to have concomitant gonorrhoea (20 per cent), 12 moniliasis and 6 condylomata acuminata. The oldest patient was aged forty years, the youngest sixteen. The average age was twenty-six years. There were 21 married and 19 single girls.

| Previous pregnancies | 0 | 1 | 2 | 3 | 4 | 5 | 8 |
|---|---|---|---|---|---|---|---|
| Number of cases | 17 | 7 | 6 | 6 | 1 | 2 | 1 |

| Duration of Pregnancy at Commencement of Treatment | Number of Cases |
|---|---|
| 1 week .. .. .. .. | 2 |
| 6 weeks .. .. .. .. | 2 |
| 2 months .. .. .. .. | 6 |
| 3 months .. .. .. .. | 3 |
| 4 months .. .. .. .. | 3 |
| 5 months .. .. .. .. | 5 |
| 6 months .. .. .. .. | 7 |
| 7 months .. .. .. .. | 2 |
| 8 months .. .. .. .. | 6 |
| 8+ months .. .. .. .. | 4 |

*Special Investigations*

Estimations of the drug in serum and urine were only performed in a few cases; the results closely resembled those found in non-pregnant women.

White blood counts were not routinely carried out in Survey I or II, as it was discovered that the counts were too variable to be of any value, especially on the out-patients. In pregnancy the white count is complicated by the fact that a leucocytosis of 12–15,000 per c.mm. is common but not constant. At parturition the count often rises to 25,000. High counts are usual in primiparae, especially in the last month of pregnancy. On the first day after delivery the count may be 17,000 per c.mm. and within a week fall to 10,000. A digestion leucocytosis is said not to occur during pregnancy.

*Results of Treatment*

There was no apparent relationship between parity or the duration of pregnancy and the subsequent clinical response. An excellent response after one course of treatment was obtained in 32 patients (80 per cent). The overall cure rate after three patients responded to a second course of tablets was 88 per cent. Spermatozoa were carefully looked for where the response to treatment was poor.

Re-infection was probably the cause of failure in 4 of the patients, 2 prostitutes who always demonstrated spermatozoa in their smears, and 2 married women who continued to have regular marital intercourse. Unfortunately both husbands refused examination or empirical treatment. Two patients with associated massive condylomata acuminata, responded to treatment only after their warts had been surgically removed. It is possible in these cases that the protozoa hide deep in the clefts of the warts and escape contact with the drug. Associated urethral warts may be responsible for re-infection of the vagina.

One patient with severe nausea and vomiting was a clinical failure due to non-absorption of the drug.

Two other failures were noted in patients with a concomitant heavy vaginal moniliasis. These cases were subsequently treated by painting the genitalia internally and externally with gentian violet and using Penotrane pessaries locally. Both drugs have trichomonacidal properties so further assessment in respect of Flagyl was invalid. On examining mixed cultures I have demonstrated in one instance trichomonads adhering by their axostyles to mycelia. It may well be that those protozoa resist or escape treatment. Where yeasts are abundant, it might be advisable to clear up this condition before commencing treatment with Flagyl which has no effect on the *Candida albicans*. Scott Gray and Murrell (1961) suggested that there might be a tendency to a slight increase of moniliasis with this drug.

A delayed clinical response was noted in one patient exhibiting an extensive acute bleeding cervical erosion. After painting the cervix with iodine and alcohol the response was good.

*Observation Period*

In December, 1960 only 26 patients in this survey were able to attend the clinic; others were recently confined or unfit to travel. The observation period of these patients was as follows:

| Time in months | 2 | 3 | 4 | 5 | 6 | 7 |
|---|---|---|---|---|---|---|
| Number of cases | 8 | 9 | 4 | 3 | 1 | 1 |

PART II. FLAGYL AND THE BABY

When this survey was conducted a few months ago, the effect of Flagyl on the foetus and the breast-fed infant was not known. No animal experimentation had been performed to determine whether a placental barrier to the drug existed. In view of the composition of the drug, this survey was considered advisable. The paediatricians were also interested as this drug, if used carelessly, might be responsible for unexplained cases of icterus gravis occurring in hospital or general practice.

Twenty-six women admitted to hospital either in the early or late stages of labour were given Flagyl, one tablet three-hourly until delivery. No side-effects were noted in any of the mothers. Maternal blood and urine were collected towards the termination of labour. Blood was immediately collected from the umbilical cord and baby urine was collected by means of plastic bags as soon as possible after birth.

Estimations of urine and blood levels were performed on 24 patients on specimens collected during labour; estimations were purposely delayed in 2 cases for 24 and 36 hours after confinement. A careful watch was kept on these patients and their infants while in hospital and later as out-patients.

This survey shows that there is no placental barrier to the drug. The rates of clearance in both mother and child were rapid. Within twenty-four hours the concentration level was minimal and complete clearance had occurred in

TABLE I

| Maternal | | | | Baby | | | | |
|---|---|---|---|---|---|---|---|---|
| Case Record | Age | No. Tablets Taken | Specimen Collection Times | Polarographic Assay g. | | Sex | Polarographic Assay g. | |
| | | | | Serum | Urine | | Serum | Urine |
| T–S .. | 35 | 5 | Labour | 6·4 | 850 | F | 4·3 | 60 |
| W–N .. | 27 | 6 | 36 hours A-L | 0 | 0 | M | 0 | 0 |
| N–S .. | 25 | 6 | 28 hours A-L | 0 | 0 | M | 0 | 5 |
| T–L .. | 36 | 6 | 24 hours A-L | 1·0 | 5 | F | 1·2 | — |
| C–N .. | 30 | 4 | Labour | 6·6 | 440 | F | 6·0 | 40 |
| MD–L .. | 26 | 2 | Labour | 2·9 | 340 | M | 2·8 | — |
| C–S .. | 20 | 2 | 5 hours A-L | 4·3 | 75 | F | 3·7 | — |
| MGN–N .. | 31 | 6 | Labour | 9·4 | 820 | F | 10·5 | 40 |
| G–N .. | 24 | 6 | Labour | 18·0 | 860 | F | 16·6 | 100 |
| L–Y .. | 39 | 3 | Labour | 7·5 | 90 | F | 5·4 | — |
| O–T .. | 30 | 4 | Labour | 3·6 | 100 | F | 2·3 | — |
| C–L .. | 22 | 5 | Labour | 3·7 | 350 | F | 4·5 | — |
| S–N .. | 27 | 2 | 3 hours A-L | — | 50 | F | — | — |
| A–I .. | 18 | 3 | Labour | 4·5 | 410 | F | 4·5 | — |
| B–W .. | 20 | 2 | Labour | 4·1 | 30 | F | 2·5 | 15 |
| D–E .. | 27 | 2 | Labour | 4·9 | 140 | F | 5·9 | — |
| P–R .. | 25 | 6 | Labour | 19·5 | 530 | M | 16·9 | 430 |
| PQR .. | 23 | 8 | 10 hours A-L | 5·4 | No spec. | M | 9·2 | No spec. |
| DN–N .. | 29 | 4 | 2 hours A-L | 6·3 | 410 | M | 5·2 | 10 |
| R–G .. | 23 | 4 | Labour | 22·7 | 70 | M | 20·2 | — |
| F–T .. | 30 | 9 | Labour | 5·1 | 430 | M | 5·2 | — |
| R–Y .. | 25 | 4 | Labour | 7·4 | 450 | F | 10·7 | 90 |
| C–E .. | 27 | 12 | Labour | 5·6 | 500 | M | 3·0 | 140 |
| R–D .. | 24 | 33 | Labour | 9·5 | No spec. | M | 6·8 | No spec. |

M=Male. F=Female. A-L=After labour. No spec.=No specimen.

thirty-six hours. Many of the baby urines, because of natural delay in their collection, showed no concentration of the drug, although the initial foetal serum level had been high.

It was of particular interest to observe with what ease the drug was absorbed during labour, as I had been informed by senior obstetrical colleagues that very little absorption occurs during labour with some drugs taken by mouth.

The results of treatment had no relationship to the patients' age (oldest 39 years, youngest 18 years), parity or sex of child. The confinements were all normal with healthy babies.

The concentration results are presented in Table I.

In view of the above findings it is unlikely that any damage to the child would take place after birth as the drug was excreted rapidly by the infant.

Serum bilirubin estimations were carried out in some cases. The average maternal level was 0·6 mg. per cent, the average baby level being 0·9 mg. per cent. Those levels were well within the safety zones. A trace of urobilinogen was found in most of the maternal and baby urines.

Macroscopic placental examinations were normal in all cases. Three placentas were histologically examined. The chorionic villi were found to be normal in size, but in one case it was noted that the capillaries were more numerous and congested. Further histological examinations are required to show if this finding is of any significance.

*Flagyl and Breast-Feeding*

I have proved in a recent series that Flagyl is secreted in breast milk—these results are being published at a later date. The amount absorbed by the infant is being personally investigated.

*Puerperal Vaginitis*

Many women report with a trichomonal vaginitis after a recent confinement. The onset of clinical symptoms in a previously asymptomatic case may be due to the presence of the lochia acting as a good culture medium, or to the resumption of sexual intercourse.

SUMMARY

Metronidazole is a new oral trichomonacide of undoubted value. In a survey of 40 pregnant women the cure rate was 88 per cent. This percentage could be raised if all the male partners were examined and treated simultaneously with their female contacts. It is specific for *Trichomonas vaginalis*. The drug has no contraceptive and no apparent treponemacidal action. A definite diagnosis of *Trichomonas vaginalis* must be made before commencing treatment.

In view of the absence of a placental barrier, and the high concentrations sometimes found in the newborn child, this drug must be used with care and under medical supervision. Courses of treatment should never be prolonged beyond ten days. A second course may be considered in certain cases of failure.

Indiscriminate use of the drug may cause severe toxic symptoms, the formation of resistant strains of the protozoa and lack of faith in a specific trichomonacidal drug. In my series and routine clinical treatments, I have encountered no such toxic symptoms.

In these two separate surveys all confinements up to date have been normal and the babies healthy. Special attention must be paid to the drug when the mother is breast-feeding.

Flagyl has many advantages over local therapy. In the later stages of pregnancy there may be difficulty in inserting pessaries; also there may be risk of introducing infection. When a co-existing gonorrhoea is present, there is greater risk of spreading infection to others or to the eyes if pessaries are used.

The 96 patients involved in these surveys preferred oral treatment to local pessaries, although Flagyl is not an invariable cure. Patients were advised to swallow the tablets whole, as mouth symptoms were more prone to develop if they disintegrated.

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# TREATMENT OF CARCINOMA OF THE VULVA WITH AN ASSESSMENT OF RESULTS

BY

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THE main contributions to an effective treatment of carcinoma of the vulva were made by Bassett (1912), Taussig (1940) and Way (1948). Bassett suggested a radical type of vulvectomy operation, Taussig applied it to a number of cases and Way subsequently extended the operation to the radical type of vulvectomy and adenectomy that is looked on as standard treatment today. Way developed his operation because he felt that the poor results of surgery were due to removal of insufficient vulvar skin, incomplete removal of the superficial lymph network and failure to remove the deep lymphatic glands. With this operation the survival rate improved considerably and it seemed as if the subject had been carried to its logical conclusion—at least from the technical and curative points of view.

Over the past few years, however, doubts have arisen about various aspects of treatment and in particular the application of radical measures to a group of patients who are usually elderly, often frail and unlikely in any case to have a further long span of life. Discussion of these matters has always been hampered by a lack of published figures and since the disease is comparatively uncommon only those working in special centres have been able to make worthwhile contributions to the literature. Reports from individual surgeons encountering sizeable numbers of cases and making a special study of the problem would probably form a better basis for discussion and it is to be hoped that such reports will come forward.

The principal matters on which the gynaecological surgeon requires guidance are the following:

(1) What is the relationship of leukoplakia vulvae to epithelioma and how should it be treated if the best interests of the patient are to be served?

(2) Is the treatment of established carcinoma of the vulva a proper function of the practising gynaecologist or should these cases be referred to a special centre as suggested by Browne (1939) and Way (1951)?

(3) What are the advantages of the extended radical operation of Way over other treatments and should it be used wherever possible? Additional questions are whether this operation is applicable to many cases and whether the primary operative mortality is too high.

(4) Is there an operation of lesser severity which will serve as well, or nearly as well, and be less exacting for both surgeon and patient? How much less efficient will such an operation be? In the same context it is asked whether local vulvectomy without gland removal is of any value at all in the poor risk patient.

(5) Do the results justify the more severe surgical measures, in that the patient gains in health and span of life anything commensurate with the mutilation of the operation and the necessary long stay in hospital? This prolonged period in hospital is recognized as a trial to the patient and something of an embarrassment to a busy gynaecological unit.

In an attempt to answer such questions and also perhaps to find some new suggestions on

treatment, all cases of carcinoma of the vulva coming to one surgeon over a fixed period of time were closely studied and followed up and the results subsequently analyzed. The series was made up of 30 cases of cancer of the vulva treated between the years 1951–1955 inclusive. Sufficient time has now passed to ensure that all have been operated on at least 5 years ago and some 10 years ago. While the total numbers are far too small to carry any statistical weight by themselves they are of value in interpreting the published results from other centres. They show the kind of results that can be expected from an ordinary gynaecological unit not specializing in cancer surgery, and they allow judgment on whether such results are adequate. They are used also to give what support they may to the clinical impressions of someone who has made a special study of these cases over a considerable length of time.

## Methods Employed

There is general agreement that radiotherapy has no place in the treatment of this disease (McKelvey, 1947; Way, 1951) and surgical treatment alone was used.

The policy was to operate on all cases except where the patient was so ill generally that she was likely to die very soon. A wide excision of the vulva and adjacent skin combined with the maximum ablation of lymph nodes and collecting lymphatics was the aim, and this was possible more often than appeared likely at the first examination.

Three different types of operation were employed.

### (a) *Local Vulvectomy*

This was used in cases where it was quite certain that the patient could stand only a minimum of surgery. Even so, the local excision was always a wide one and corresponded more with what American surgeons call a radical vulvectomy. A generous "ear" of skin and its lymphatics were excised in a direction upwards towards the inguinal ligament on each side and sometimes enlarged glands were removed in continuity with this upward flap of tissue.

### (b) *Vulvectomy with Gland Removal as Far as the Femoral Canal*

The skin area removed and the extent of vulvar excision were exactly as in the radical (Way) operation. The superficial glands and fat with a segment of the great saphenous vein and its tributaries were dissected medially *en bloc*, and the inguinal canal then opened and explored. The transversalis fascia was incised to give access to the deep femoral group and Cloquet's gland was removed. It was considered necessary to go above the inguinal ligament to gain access to this gland which nearly always occupies the upper part of the femoral canal and, as Rentschler (1929) pointed out, the upper pole often projects into the pelvic cavity. In the earlier cases the inguinal ligament was not divided but it was soon apparent that a complete exposure of this region could not be obtained without first detaching the inguinal ligament from the pubes.

### (c) *Extended Radical Vulvectomy Operation*

This operation was considered the procedure of choice and as time passed and results were observed it appeared the most efficient. The technique described by Way was closely followed in all essentials. It was considered necessary to remove the superficial and deep inguinal and femoral glands, the obturator glands, the external iliac and hypogastric nodes, and any glands around the bifurcation and lower part of the common iliac artery. Provided the patient's general condition was satisfactory there was no technical difficulty in removing these glands.

Except at the beginning of the series all the operations were done under general anaesthesia using hypotensive drugs. Hexamethonium was used in some and Arfonad in others and the effects were similar. There were initial doubts about the wisdom of using such agents in frail old people but these were quickly dispelled. With ordinary care there seems to be little danger in giving these drugs and the benefits to the patient are very great. Bleeding is so much reduced that there is seldom the need for more than one supportive pint of blood and several patients required none at all. The systolic blood pressure during operation is depressed to about 60 or

70 mm. of mercury and is allowed to rise towards the end of the operation. In an hour or two the blood pressure is back to normal and there is no subsequent tendency to collapse or fall in blood pressure.

The very large areas denuded of skin in such radical operations were treated by skin grafting. Intermediate thickness skin grafts were cut from the lateral aspect of the thigh at the time of operation and applied. This reduced the amount of plasma lost from raw areas and prevented further traumatic shock. The main purpose of grafting was to accelerate healing and this it undoubtedly did. It was estimated that it halved the time the patient would otherwise have to spend in hospital. The freshly grafted areas were covered with tulle gras and sealed off with a pressure dressing which was not disturbed for at least 5 days.

A Foley catheter was inserted into the bladder and the end brought out through the sealed off dressing. Antibiotics were given routinely for 7 days and the patient got out of bed on the first post-operative day. Baths were allowed by about the 10th day and thereafter became a daily routine.

## Results

There were 30 cases altogether and they provided a representative sample of the disease. Most of the patients were in the older age group but 7 were in the fourth decade. Ten growths were of fungating and 20 of malignant ulcer type and some of the former were quite huge in size. The commonest site of the primary growth was the labium majus, while the clitoris was the next most frequent, and the anus was involved in 4 cases. Eighteen patients showed evidence of previous or accompanying leukoplakia vulvae and there may well have been more than that. There were 28 squamous cell carcinomata, one adenocarcinoma arising in Bartholin's gland and one malignant melanoma.

When instituting treatment (Table I) only one patient was considered quite inoperable and she died a few days later. Four were clearly unfit for anything but the minimum of surgery and operation A was employed. Twenty-five patients were considered fit for major surgical procedures

Table I

*Details of Treatment Employed*

| | |
|---|---|
| Total cases | 30 |
| Operability: | |
| Inoperable | 1 |
| Fit for minimal surgery | 4 |
| Operable | 25 |
| Operation done: | |
| A. Local vulvectomy | 4 |
| B. Vulvectomy with removal of inguinal and femoral but not iliac glands | 11 |
| C. Vulvectomy with removal of inguinal femoral and iliac glands (Way) | 14 |
| Preliminary colostomy (2 subsequently closed) | 3 |
| Operative or post-operative deaths | 1 |
| 5-year survivals (63·3%) | 19 |

and operation B was done on 11 and operation C on 14. Preliminary colostomy was done in 3 cases to allow of removal of the anal growth, and of these 2 subsequently had bowel function restored, and the other retains the colostomy because the sphincter mechanism had to be completely removed. Incidental surgical procedures such as removal of the terminal part of the urethra or repair of inguinal hernia were occasionally done at the time of operation but only when necessary either for removal of the disease or to aid recovery. Complications were few, but included 2 cases of osteomyelitis of the pubes. They both made good recoveries. In only 4 cases did the pathologist report gland involvement and of these 2 had inguinal glands affected and 2 had deep femoral node involvement. This is a very low figure indeed and is not explained by any cursory examination of the tissue removed. The specimens were most carefully sectioned and examined and as many as 12 individual glands were sectioned and examined in some cases.

Of the 30 cases 15 have died and 15 survive and Tables II and III give the relevant information on the 2 groups. It is seen that 3 of the local vulvectomy cases have died although one survived for 5 years, another for 2½ years and the third for 6 months. Of the 11 cases where operation B was done, 6 have died, and it will be noted that every single one of these patients died of pelvic or abdominal secondaries. In that group only one patient was reported as having

TABLE II

*Analysis of Deaths*

(Number=15)

| Year First Seen | Name | Age at Death | Operation | Survival Time | Cause of Death | Recurrence |
|---|---|---|---|---|---|---|
| 1950 .. | E.S. | 73 | A | 6 months | Cardiac failure | No |
| | G.H. | 47 | B | 3 months | Pelvic secondaries | Yes |
| | Ch.D. | 67 | B | 1 year | Pelvic secondaries | Yes |
| | A.D. | 72 | A | 6 years | Myocardial failure | No |
| | F.H. | 77 | — | 3 weeks | Massive primary | — |
| | Cl.D. | 49 | B | 9 months | Pelvic secondaries | Yes |
| 1952 .. | M.N. | 55 | B | 2½ years | Abdominal secondaries (liver) | Yes |
| | C.B. | 69 | B | 5 years | Myocardial degeneration and senility | No |
| | S.C. | 80 | B | 3 years | Pelvic secondaries | Yes |
| | M.W. | 67 | C | 7 years | Coronary thrombosis | No |
| 1954 .. | K.R. | 80 | C | 5 days | Post-operative pneumonia | — |
| | H.H. | 43 | C | 9 months | Brain secondaries (malignant) (melanoma) | Yes |
| 1955 .. | M.H. | 68 | C | 2½ years | Bronchial carcinoma (probably primary) | No |
| | E.F. | 78 | A | 3 years | Cardiac failure | Yes (Local) |

TABLE III

*Analysis of Survivals*

(Number=15)

| Year First Seen | Name | Present Age | Operation | Survival Time |
|---|---|---|---|---|
| | | | | (Years) |
| 1950 .. | M.W. | 60 | B | 10 |
| | N.T. | 80 | B | 10 |
| | M.C. | 51 | B | 10 |
| 1951 .. | G.G. | 56 | B | 10 |
| | E.F. | 91 | B | 10 |
| | M.J.T. | 44 | C | 9½ |
| | E.H. | 63 | C | 9½ |
| 1953 .. | E.J. | 75 | C | 8 |
| | B.H. | 55 | C | 7½ |
| 1954 .. | M.K. | 76 | C | 7 |
| 1955 .. | E.W. | 77 | C | 5 |
| | M.J.M. | 85 | A | 5 |
| | F.S. | 85 | C | 5 |
| | A.R. | 65 | C | 5 |
| | A.F. | 77 | C | 5 |
| | F.K. | 78 | C | 5 |

gland involvement. Of the 14 extended radical vulvectomy cases 4 have died. One developed post-operative pneumonia at the 3rd day and died 2 days later. She was a patient with a history of chest trouble and did not have routine post-operative antibiotics. I considered the omission largely responsible for her pneumonia and this was probably an avoidable death. The second was the case of malignant melanoma who actually survived 9 months and that must be about the maximum reprieve one could expect in the circumstances. The third was interesting in that she survived 2½ years and then died of bronchial carcinoma which may or may not have been primary, but at post-mortem examination there was no evidence of local or pelvic secondaries from the vulvar lesion and the pathologist thought the two cancers unassociated. The fourth was the case of Bartholin's gland adenocarcinoma. She survived 7 years and died of coronary thrombosis. There was no recurrence of the malignant condition.

The number of patients surviving 5 years or more is 19 (63·3 per cent). Apart from 6 who have just had time to bridge the 5-year gap, one has survived for 7 years, one for 7½ years,

one for 8 years, two for 9½ years, and five have survived 10 years. This is really quite astonishing when one considers the average age and the many ills that might well befall them.

## Discussion

### (1) *Leukoplakia Vulvae*

Most people are agreed that leukoplakia vulvae predisposes to epithelioma and that in time the skin lesion will develop areas of malignancy. Jeffcoate (1957) is not convinced that epithelioma occurs more frequently in patients with leukoplakia than in those without and thinks that any chronic skin disease or irritation might equally well predispose to it. Taussig (1940) reported leukoplakia present in 6 per cent of his cases of vulvar cancer, and Way (1951) in 82 per cent. Green *et al.* (1958) found an incidence of 58 per cent but the figures were very incomplete and the true incidence must have been 72 per cent at least. In the series reported here leukoplakia was present in 60 per cent of cases.

There is certainly a great deal of confusion about the term leukoplakia, and Jeffcoate very rightly points out that it is a clinical and not a histological diagnosis. The conditions most likely to be confused with it are kraurosis vulvae and what the dermatologists call lichen sclerosis. There should be no difficulty in distinguishing kraurosis with its smooth red skin progressing to an atrophic contracted condition with introital narrowing. Lichen sclerosis is less easy to distinguish but the main features are the general redness and moistness of the vulva and the surface infection. The white areas are less white and the fissures less deep than in leukoplakia which has a much drier appearance. The ultimate decision on the danger of the leukoplakia depends on the biopsy findings and it is really at this point that the treatment of carcinoma of the vulva begins. In all cases where there is the possibility of metaplasia, biopsy should be done and repeated as often as is necessary. Figure 1 shows a leukoplakia vulvae where biopsy revealed intra-epithelial carcinoma with one area of invasion. There was widespread carcinoma *in situ* in the sections of the removed vulva and the local malignant condition recurred 4 years later despite wide vulvectomy. Figure 2 illustrates a transition from leukoplakia appearances to frank malignancy in a single section and is a reminder of this ever-present danger. The treatment of leukoplakia vulvae when biopsy shows any shift towards malignancy is to remove the vulva locally with a wide but not necessarily deep area of skin. Quite apart from anticipating epithelioma the operation relieves the patient of a most distressing pruritus.

### (2) *Location for Treatment*

Considering that the individual gynaecologist will rarely operate on more than two of these cases in a year and his nursing staff do not have the opportunity of establishing a set routine, there would seem to be a case for transferring these patients to a special centre if the best results are to be obtained. Practical considerations, however, outweigh these theoretical arguments. Elderly people will generally refuse to be transported from their homes to some distant clinic with cancer associations and it would be unreasonable to insist on it. It is essential for them that they keep in touch with their children and relatives on whom they are totally dependent. The obvious place for treatment is the local hospital which they know, and there is usually no difficulty in persuading them to go somewhere near at hand and where they know they can be visited.

The management of such cases is within the scope of any gynaecological unit and the speciality is narrow enough without encouraging further shrinkage unless there is good reason for it. Surgeons and nurses alike enjoy the challenge of the work and the elderly patients, being special problems among younger people with more ordinary troubles, develop a feeling of importance and wantedness which sustains them and hastens their recovery. Working in such conditions the results in this series are comparable with the published results from special centres and even if they did compare less favourably, this is surely a place where a fractional advantage in surgical efficiency might well be sacrificed. They are immensely grateful patients who attend for follow-up examination meticulously, and the hospital becomes one of

FIG. 1

Leukoplakia vulvae presenting dangerous appearance. Biopsy revealed malignant change.

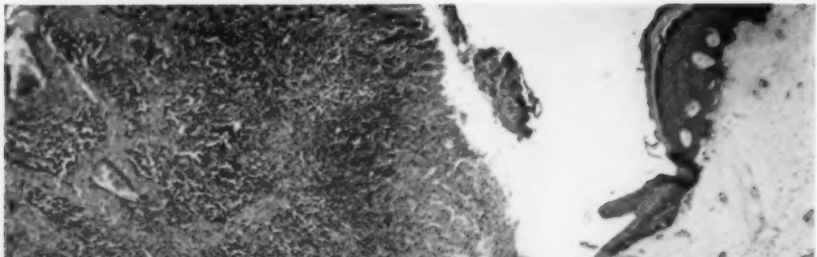

FIG. 2

Squamous-celled carcinoma of vulva arising in leukoplakia vulvae. From right to left the second stage leukoplakia is seen to progress through basal cell hypertrophy and surface ulceration to invasive carcinoma and necrotic growth. H. & E. ×4·5.

the focal points in their lives. The case for local treatment and care of these patients is certainly a very strong one.

### (3) *Advantages of the Radical Extended Operation*

The advantages claimed for the extended radical vulvectomy of Way are that a wide area of vulvar skin is removed and all the glands and lymph pathways likely to be affected are excised. From the nature of the disease the whole vulvar skin area is liable to further epitheliomatous change and this has been shown to occur where skin removal is limited. It is virtually impossible to find out which glands are involved by malignancy either clinically or histologically and since the line of advance of the disease is so well known it must surely be correct to "head off" this advance as far forward as is practicable—namely at the level of the bifurcation of the common iliac artery. That the radical extended operation is the treatment of choice is emphasized by those who have studied the largest number of cases.

Way (1951), Collins *et al.* (1951, 1956) and Green *et al.* (1958) all say that adequate surgical treatment means a wide vulvectomy, groin dissection preferably in continuity, and removal of the deep glands up to the common iliac trunk. They are convinced from their statistics that nothing else will give maximum cure rate and Green *et al.* reckon the 5-year survival rate is increased two-and-a-half fold by such surgery. Payling Wright (1958) adds further support when writing on the recurrence of tumours generally after extensive surgical treatment. Recurrence he says is almost always due to incomplete resection and arises in microscopic groups of malignant cells left behind or even cut through in the line of resection. He reminds us that the area of tissue affected by pre-cancerous change may be much larger than that actually removed so that further primaries may develop close by. Such general observations are particularly apposite to this region of the body, where susceptible tissue and lymph drainage pathways are peculiarly suited to a policy of wide ablation.

The results from operation C in this series are very much better than from the other procedures and analysis of the 4 deaths does not show any valid criticism of the operation.

The objections to its routine use are the low operability and high mortality rates. For example Way's operability rate was 87 per cent and, while he admittedly tackled poor risks, his operative mortality was 14·9 per cent. Such a mortality rate is too high for most surgeons and this has made them wary of doing the operation. As a result various inadequate operations have been used with less satisfactory results on patients who should have had the advantage of the radical procedure. Fortunately there is now available a new factor which transforms the situation and that is the use of the hypotensive technique in anaesthesia. Using this method it is safe to do radical extended vulvectomy in all but the frailest and most ill patients and with a negligible mortality. The patients are exceedingly well post-operatively and all concerned with their treatment and nursing are convinced that shock is reduced or circumvented in some way. This of course has been noted in other surgical fields where hypotensive anaesthesia has made possible operations which formerly could not be attempted. There is no satisfactory physiological explanation of how the benefit is obtained, but it is very real. The surgeon finds the operation immensely easier and it becomes a safe and controlled dissection unobscured by blood. The operation takes less time, involves less trauma and is more complete. The method was used in all the later cases in this series. There was only the one post-operative death, and that probably avoidable.

### (4) *The Place of Limited Operations and of Local Vulvectomy*

The reason for employing a less radical operation was the high mortality of the complete procedure but this was not always admitted and various reasons have been put forward for not doing a deep dissection of glands. That is the part of the operation one is most tempted to omit since the dangers of massive haemorrhage when separating enlarged glands from the external iliac artery and vein are all too evident to the operator. It is true also that wide tissue exposure in the extra-peritoneal region is necessarily associated with considerable shock

and it is attractive to avoid that. Taussig (1940) had reported that there was no difference in the survival rate of cases whether the glands were involved by malignancy or not. Watson and Gusberg (1946) found the high glands infrequently involved by growth and Bibby (1957), in a review of Currie's cases, took the view that even if they were, it was probably not justifiable to remove them in view of the high operative mortality involved in doing so. Currie used a limited operation in which the deep glands were not removed and a bridge of skin was retained between vulva and groins to allow of quicker healing and shortened convalescence and he showed very good results.

The main argument against these operations is that we do not know how often the deep glands are involved. Even if the excised tissue is available for section the pathologist cannot section it all and positive reports often refer to a microscopic area of malignancy in a single gland. It is unfortunately true also that pelvic secondaries sometimes develop in cases where no gland involvement was reported in the tissue removed. Perhaps most important of all is the fact that virtually all lymph drainage from the vulva passes through the deep femoral nodes and the removal of this group of glands is paramount. These glands lie above or behind the inguinal ligament and the view is most strongly held that they cannot be adequately exposed from below and that it is essential to open up the femoral canal. Any operation omitting removal of this group of glands is dangerously incomplete.

Way (1957) has recently been experimenting with a method whereby he takes smears from the lowest gland of the deep group and the extent of the operation is determined by the results of the cytological examination. Such methods depend on having a whole department and laboratory geared to one's own needs and can only be obtained in a special centre. Green (1957), on the other hand, points out that deep pelvic node dissections add little to the difficulty, risk, or time consumed in doing the total operation and he prefers to incorporate them into his standard procedure, rather than adopt frozen section or cytological smears of Cloquet's gland. He considers that since over half of the patients have involved lymph nodes, the less complete operation will only occasionally be sufficient to cure.

In this present series a compromise operation (operation B) was used for a time, and until safer conditions were found for the radical procedure. It is seen from the follow-up of these cases that every one of the 6 patients who died had pelvic or abdominal secondaries although in only one was gland involvement reported by the pathologist.

The conclusion reached is that this type of operation may serve well enough in some circumstances but it is considerably less efficient than the extended radical vulvectomy. With the availability of new anaesthetic techniques making major surgery available to so many more patients there would seem to be little place for the less complete operations.

Local vulvectomy is a policy dictated by necessity but its extent can be modified and obviously the widest excision possible should be done. Some patients survive for quite a long time although the most one expects is a period of relief from symptoms. Of the 4 done in this series (operation A) one has survived over 5 years.

(5) *Evaluation of Treatment*

The published results of treatment fully justify the use of major surgery in the treatment of this disease; and as advances in technique make conditions safer the advantages to the patient will be increased.

The 5-year survival rates reported by Way (1951), Collins *et al.* (1956) and Green *et al.* (1958) are excellent and if a patient survives 5 years it is likely that she is clear of the disease and many such have a 10 or 15 or even 20 years further span of life. It is interesting to note that the Registrar General's figures give a life expectancy of a further 5 years at the age of 80. But that is not the sole advantage gained and one might consider deliverance from the pain and stink and humiliation of such an affliction even for a short spell an equal blessing.

The operation is far less mutilating than one would expect and, despite the large area of skin removed, there are no locomotory or urinary complications. Quite a proportion of patients

subsequently develop prolapse and the vulvectomy must be held responsible for that, but repair presents no special difficulty.

The length of time spent in hospital is a difficulty for patient and hospital but this has in large part been overcome by using immediate free skin grafts. McKelvey (1955) and Way (1957) report that free skin grafting is quite useless because of the unavoidable sepsis in these wounds but the policy has been most successful in this series. While it is likely that some degree of superficial wound infection will develop it is not immediately present and does not prevent the grafts from adhering. The degree of "take" is high and generally in excess of 50 per cent. At the very worst one gains valuable islands of epithelialization over the raw area and the squamous cells rapidly reduce the space when advancing on so many fronts from so many bases. Schaeffer *et al.* (1955) used similar methods in the treatment of leukoplakia and carcinoma of the vulva and reported a high percentage of "take", rapid healing, and greatly improved results. In the present series the patients who had skin grafts went home in 6 weeks or sooner with perhaps a covering dressing on a small clean healing area. The average time spent in hospital for the whole series worked out at 9 weeks, but this was greatly inflated by 2 cases in which I attempted flap grafts of the type suggested by Way (1955) and by Charles (1955). The flap grafts tend to suffer from an inadequacy of blood supply at the periphery probably because the vessels have to run upwards into the flap and this is always unfavourable. There is also some twist or rotation on the flap which further jeopardizes the blood supply. When one considers the atheromatous and calcified state of the large vessels in these old people it is not surprising that the formation of capillaries at the distal edge of an undercut flap of skin is beyond their powers. The freeing of skin in this way is a shock-producing procedure at the end of a major operation and Schaeffer considers that delayed healing with induration is a frequent complication if one attempts to undermine the skin. Intermediate thickness skin grafts can be cut quickly and easily and instead of causing shock they go a considerable way to lessening it by preventing serum loss from the raw area. This type of skin grafting is of immense benefit in speeding recovery and improving the final result.

## Summary

(1) Problems outstanding in the treatment of carcinoma of the vulva are listed for study.

(2) The methods of treatment employed in a personal series of 30 cases are set out. Hypotensive anaesthesia and skin grafting were extensively employed.

(3) The results in the series are analyzed in relation to the type of operation used.

(4) The problems listed in (1) are discussed in the light of published reports and the experience of this study.

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# FOETAL WEIGHT, PRESENTATION AND THE PROGRESS OF LABOUR

## Part I—Occipito-anterior: the Effect of the Baby's Weight upon Labour

BY

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### INTRODUCTION

THE length of the first stage of labour is determined by many factors. Medical opinion is attracted now to one aspect, now to another and gradually fallacies are disproved and abandoned. One such idea, however, dies but slowly, namely that a large baby has an adverse effect upon the length of the first stage of labour.

In order to establish the precise effect which foetal weight has upon the duration of labour—if indeed it has any effect at all—the records of some 6,000 deliveries at University College Hospital have been submitted to statistical analysis. The interest being primarily in the first stage, those cases where that is ill-defined, e.g., Caesarean sections and oxytocin infusions, were omitted. The important factor being foetal weight, all abnormal presentations were omitted lest that very condition and not the baby's weight should be the determining factor in the length of labour. Multiple pregnancies were also excluded. Interesting facts concerning the weight of the babies presenting abnormally are dealt with separately in Part II.

The subject of this paper is therefore the length of the first stage of labour in primiparae and multiparae separately for the delivery of small, average and large-sized babies presenting by the vertex, either left or right occipito-anterior. Other aspects of labour are mentioned and some complications of labour, commonly supposed to be influenced by the size of the baby, are shown to be associated with each other quite independently of foetal weight.

The analysis of a large volume of data by semi-automatic means and the discovery of statistically significant relationships between factors leads, of necessity, to some trite observations and emphasizes correlations which are due only to the treatment administered.

The impersonal approach does, however, enable correlations to be discovered which were unsuspected and on occasion throws new light on old adages by emphasizing the importance of a third intervening factor.

The presentation of knowledge gathered in this way is most constructively related to other investigations or to experience if the data are given fully and the conclusions presented without attempt at interpretation or justification. Where complex interrelations exist between a number of factors new methods of presenting the data are needed and the diagrams attempt to bring a large compass of information into one intelligible setting.

### SOURCES, METHODS AND CRITERIA

The data for this survey were drawn from the records of the 6,000 deliveries which took place

at University College Obstetric Hospital from 1953 to 1957. The data were analyzed by the method of Smyth and Bainbridge (1957) in which the information is divided into groups and not treated as continuous variables. All vertex occipito-anterior babies were accordingly divided into three weight groups: under 6 pounds (2,700 g.) but at least 28-weeks maturity; 6 to 8 pounds; and over 8 pounds (3,600 g.), our aim being to include all the babies of average size in one group. We found that 8 pounds (3,600 g.) is too low a limit for a "big" baby and in any future investigation we should raise it by half a pound (222 g.). We originally had 4 groups but smallness of numbers compelled us to amalgamate two.

After Caesarean sections, pitocin infusions, multiple deliveries and abnormal presentations were excluded, the number remaining was:

| | Over 8 Pounds (3,600 g.) | 6–8 Pounds | Under 6 Pounds (2,700 g.) | Total |
|---|---|---|---|---|
| Primiparae .. | 699 | 2,117 | 278 | 3,094 |
| Multiparae .. | 671 | 1,163 | 171 | 2,005 |

For a full list of the factors studied we refer readers to Table II. We were unfortunately compelled to omit the very relevant study of relative disproportion because of unreliability of data.

Multiparous patients admitted to the hospital are not representative of the population, being admitted for obstetric indications or social reasons.

## Definition of Terms

(1) Onset of labour is taken as the first painful contraction; an attempt to time it by dilatation proved impracticable since about half of our patients are 2 or 3 cm. dilated before the first painful contraction, or before admission to hospital.

(2) The length of the second stage is approximate only.

(3) Post-partum haemorrhage is estimated, not measured.

(4) "Raised blood pressure" is defined as diastolic of 95 mm. Hg at least once in pregnancy and therefore includes hypertensives and toxaemics indiscriminately.

(5) Foetal distress is defined as a heart rate less than 100 or more than 160, or gross irregularity, or passage of thick meconium.

On the graphs, those points which differ from the mean (i.e., the average of the two or three groups shown together on each diagram) at the 5 per cent level of significance have been encircled, and those in which the number of patients was too small for the test of significance to be applicable have been boxed—although it should be emphasized that these figures are just as relevant as the rest.

## Parity and Length of Labour

Although there is undoubtedly a great deal of justification for the usual practice of grouping patients into primiparae and multiparae, we thought it advisable to verify that in length of first stage all multiparities are sufficiently similar to justify continuing this practice.

Table I

*Mean Length of First Stage, in Hours*

| | Total | Over 8 Pounds (3,600 g.) | 6–8 Pounds | Under 6 Pounds (2,700 g.) |
|---|---|---|---|---|
| Primiparae .. | 17·1 | 18·6 | 16·9 | 15·6 |
| Multiparae .. | 11·1 | 11·2 | 10·9 | 12·1 |
| Para-1 .. .. | 11·2 | 11·3 | 11·0 | 13·0 |
| Para-2 .. .. | 11·1 | 12·1 | 10·1 | 12·7 |
| Para-3 .. .. | 9·6 | 8·3 | 10·3 | 10·2 |
| Para-4 .. .. | 10·1 | 9·9 | 10·9 | 6·9 |
| Para-5+ .. | 8·8 | 8·8 | 8·4 | 6·8 |

This shows that after the great change between para-0 and para-1 there is a gradual reduction in the length of labour. The variance is also reduced (Fig. 1). As there is no very marked difference between the multiparities below "para-5" we are satisfied to continue the custom of dealing with them together.

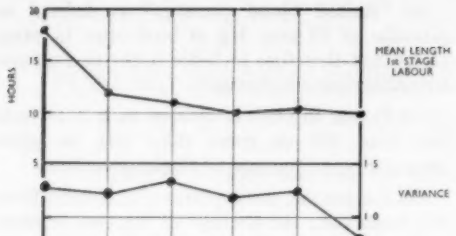
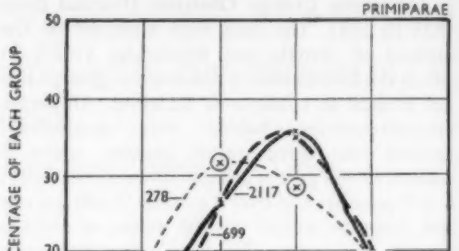



FIG. 1

Effect of parity upon the length of labours.



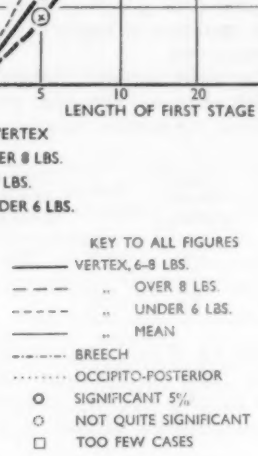




FIG. 2

Lengths of labour for three foetal weight groups, primigravidae.

Key applicable to Figure 2 and to succeeding diagrams in Part I and in Part II.

## PRIMIPARAE

*Length of First Stage*

Figure 2 illustrates the distribution of labours in the three weight groups:

It will be seen that:

(1) In the shortest labours there is a greater than average number of small babies and in the longest labours a greater than average number of large babies.

(2) With the smallest babies, 21·32 per cent of primiparae, the most common time taken (i.e., the mode) is about 12 hours, the mean duration being estimated at about 15·6 hours.

(3) The middle group represents 68·38 per cent of all primiparae and therefore comes very close to the average; here the mode is about 20 hours and the average duration 16·9 hours.

(4) In the third group, babies greater than 8 pounds (3,600 g., 8·98 per cent of primiparae) the significant lack of very short labours and the converse significant increase in the number of patients in the long labour group should not blind us to the remarkable similarity to the normal occurring between these two extremes. The mode is about 17 hours, 3 hours lower than in average-sized, and the mean duration of the first stage about 18·6 hours.

Thus we find a lengthening of the first stage as the weight of the baby increases. It is possible to express our findings in two other ways: taking 30 hours as the maximum length for normal labour (Ostrey, 1955; Calkins, 1955) we find:

90·7 per cent of first stages in the under 6 pounds (2,700 g.) group were completed before 30 hours.

89·2 per cent of first stages in the 6–8 pounds group were completed before 30 hours.

85·0 per cent of first stages in the over 8 pounds (3,600 g.) group were completed before 30 hours.

Or, 90 per cent of patients whose babies weighed less than 6 pounds (2,700 g.) completed the first stage by 30 hours, by 32 hours where the babies weighed from 6 to 8 pounds and by 37 hours where they weighed more than 8 pounds (3,600 g.). Thus the occurrence of "long labour" increases with the size of baby; we should, however, be careful to avoid deducing from this that "big babies mean long labours"—since as many as 85 per cent of large babies are delivered after first stages of normal length.

Before leaving the first stage we should comment upon raised blood pressure which is known to influence the length of labour and is twice as common in mothers whose babies weigh less than 6 pounds. We found that:

| | Over 8 Pounds (3,600 g.) | 6–8 Pounds | Under 6 Pounds (2,700 g.) | |
|---|---|---|---|---|
| | % | % | % | |
| Normal blood pressure .. | 85·2 | 88·9 | 91·1 | delivered by 30 hours |
| Raised blood pressure .. | 84·0 | 93·0 | 88·0 | delivered by 30 hours |

Thus raised blood pressure does not shorten labour in the group in which it occurs most and therefore does not affect our previous conclusion.

*Effect of the Baby's Weight upon Factors Other than Length of First Stage*

The percentage incidence of 13 factors in the three weight groups and the deviations which they make from the average are shown in Tables IIa, b and c. Only three factors appear to be

TABLE IIa

| | Primiparae | | | | Multiparae | | | |
|---|---|---|---|---|---|---|---|---|
| | Total | >8 Pounds (3,600 g.) | 6–8 Pounds | <6 Pounds (2,700 g.) | Total | >8 Pounds (3,600 g.) | 6–8 Pounds | <6 Pounds (2,700 g.) |
| 1st Stage: | % | % | % | % | % | % | % | % |
| Over 80 hours .. | 0·16 | 0·1* | 0·14* | 0·4* | 0·25 | 0·3* | 0·26* | 0* |
| 80— .. .. | 5·68 | 7·9+ | 5·15— | 4·3 | 2 | 2·2 | 1·72 | 2·9* |
| 40— .. .. | 19·51 | 20·3 | 19·37 | 18·7 | 8·93 | 7·6 | 9·11 | 12·9 |
| 20— .. .. | 35·63 | 36·3 | 36·42 | 28·1 | 25·24 | 27·3 | 24·5 | 22·2 |
| 10— .. .. | 27·0 | 26·7 | 26·45 | 32·0 | 32·07 | 31·4 | 32·41 | 32·2 |
| 5— .. .. | 11·95 | 8·6— | 12·47 | 16·6+ | 31·52 | 31·1 | 31·98 | 29·8 |
| 2nd Stage: | | | | | | | | |
| 2+ hours .. | 5·98 | 10·4+ | 4·91— | 2·9— | 0·49 | 0·7* | 0·34* | 0·6* |
| 2— hours .. | 39·73 | 49·2+ | 38·3— | 27·0— | 7·33 | 10·3+ | 6·36— | 2·3— |
| ¾— hour .. | 47·06 | 36·6— | 49·79+ | 52·9+ | 44·94 | 50·5+ | 42·65— | 38·6 |
| ¼— hour .. | 7·17 | 3·7— | 6·99 | 17·3+ | 47·24 | 38·4— | 50·64+ | 58·5+ |
| 3rd Stage: | | | | | | | | |
| 1+ hours .. | 2·16 | 1·9 | 2·17 | 2·9 | 2·09 | 1·9 | 1·72 | 5·3* |
| 1— hour .. | 1·74 | 1·4 | 1·94 | 1·1* | 1·3 | 0·9 | 1·29 | 2·9* |
| ½— hour .. | 4·49 | 5·0 | 3·97— | 7·2+ | 4·69 | 4·0 | 4·73 | 7·0 |
| ¼— hour .. | 91·54 | 91·7 | 91·92 | 88·9 | 91·93 | 93·1 | 92·26 | 84·8— |

Vertex Presentations

\+ or — denotes significant relationship at 5 per cent level.
* denotes too few patients for statistical analysis.

TABLE IIb

| | Primigravidae | | | | Multigravidae | | | |
|---|---|---|---|---|---|---|---|---|
| | Total | >8 Pounds (3,600 g.) | 6–8 Pounds | <6 Pounds (2,700 g.) | Total | >8 Pounds (3,600 g.) | 6–8 Pounds | <6 Pounds (2,700 g.) |
| Age: | | | | | | | | |
| 40+ .. .. .. | 0·61 | 0·6 | 0·61 | 0·7 | 4·09 | 4·0 | 3·87 | 5·9 |
| 40— .. .. .. | 3·33 | 2·9 | 3·31 | 4·7 | 11·72 | 12·2 | 11·52 | 11·1 |
| 35— .. .. .. | 11·89 | 11·0 | 12·09 | 12·6 | 28·03 | 30·1 | 27·0 | 26·9 |
| 30— .. .. .. | 33·5 | 33·2 | 34·25 | 28·8 | 33·42 | 33·1 | 34·05 | 30·4 |
| 25— .. .. .. | 41·51 | 44·2 | 40·58 | 42·1 | 20·75 | 19·2 | 21·15 | 24 |
| 20— .. .. .. | 9·11 | 8·2 | 9·16 | 11·2 | 2·0 | 1·3 | 2·41 | 1·8* |

+ or — denotes significant relationship at 5 per cent level.
* denotes too few patients for analysis.

TABLE IIc

| | Primigravidae | | | | Multigravidae | | | |
|---|---|---|---|---|---|---|---|---|
| | Total | >8 Pounds (3,600 g.) | 6–8 Pounds | <6 Pounds (2,700 g.) | Total | >8 Pounds (3,600 g.) | 6–8 Pounds | <6 Pounds (2,700 g.) |
| Post-partum haemorrhage: | | | | | | | | |
| 20+ ounces .. | 3·2 | 7·2+ | 2·08— | 1·8 | 3·54 | 4·6 | 2·92 | 3·5 |
| 19— ounces .. | 14·34 | 17·3+ | 13·84 | 10·8 | 15·01 | 18·5 | 13·33+ | 12·9— |
| 10— ounces .. | 82·4 | 75·5— | 84·08+ | 87·5+ | 81·45 | 76·9 | 83·74— | 83·7+ |
| Surgical induction .. | 13·4 | 14·4 | 12·75 | 15·8+ | 13·47 | 15·2 | 12·64 | 12·3 |
| Hypertensive .. .. | 8·66 | 7·2 | 8·27 | 15·5+ | 8·03 | 8·8 | 7·48 | 8·8 |
| Forceps .. .. | 5·88 | 10·3+ | 4·72— | 3·6 | 1·3 | 1·6 | 0·95 | 2·3* |
| Manual removal .. | 3·0 | 2·7 | 3·07 | 3·2 | 2·69 | 2·2 | 2·41 | 6·4* |
| Foetal distress .. .. | 8·08 | 6·9 | 8·03 | 11·5+ | 4·49 | 4·0 | 4·47 | 6·4 |
| Stillbirths .. .. | 1·29 | 0·4— | 0·28— | 11·2* | 1·25 | 0·1— | 0·95 | 7·6* |
| Sex: | | | | | | | | |
| Male .. .. .. | 51·87 | 59·2+ | 50·12— | 47·2 | 51·13 | 60·6+ | 46·95— | 42·1— |
| Female .. .. | 48·06 | 40·8— | 49·88+ | 52·9 | 48·88 | 39·3— | 53·05+ | 57·9+ |
| Head circumference: | | | | | | | | |
| Over 36 cm. .. | 17·67 | 35·5+ | 13·89— | 1·8— | 20·45 | 40·9+ | 11·26— | 2·3— |
| Under 36 cm. .. | 82·27 | 64·5— | 86·11+ | 98·3+ | 79·56 | 59— | 88·73+ | 97·7+ |

Vertex Presentations

+ or — denotes significant relationship at 5 per cent level.
* denotes too few patients for statistical analysis.

unaffected by weight, namely, length of the third stage, manual removal of the placenta and the mother's age. Karn and Penrose (1951), working on a much larger series and in much narrower groupings, found that the weight of first babies decreases with increasing age.

The remaining factors do show some relationship to baby's weight. It can clearly be seen in the Table that a long second stage, an increased post-partum haemorrhage, and forceps deliveries, occur more amongst the larger babies but, on the other hand, there is an absence of stillbirths. It is amongst the smallest babies that intra-partum as well as ante-partum deaths occur most frequently, and also foetal distress.

The figures cannot, however, be used to prove that greater weight in itself is the *cause* of forceps or post-partum haemorrhage or other apparently related factors. Although it is certainly possible that the increase of some factor *may* be due to greater weight, the cause may equally well be some third factor which occurs more frequently in one group than in the others. For example, the increased post-partum haemorrhage may be caused by greater size of baby or by the anaesthetics and forceps deliveries which are more frequent in that group.

In order to distinguish cause from effect further investigation of data was needed; consequently every combination of two factors was analyzed in each weight group. Some relationships were found to be significant in all three groups, that is to say, they remain related no matter what the weight of the baby, so that weight of baby must be eliminated as the causal factor. These relationships are as follows:

Long first stage is associated with long second stage and forceps;

Short first stage is associated with raised blood pressure and surgical induction;

Long second stage is associated with long first stage, forceps, head over 36 cm. in circumference;

Long third stage is associated with post-partum haemorrhage and manual removal of placenta;

Short third stage is associated with forceps and big head;

Increased post-partum haemorrhage is associated with forceps, manual removal of placenta and long third stage;

Forceps is associated with long first stage, long second stage, short third stage, post-partum haemorrhage, big head, greater maternal age, foetal distress;

Head circumference over 36 cm. is associated with long second stage, short third stage, forceps, males and foetal distress;

Manual removal of placenta is associated with long third stage, post-partum haemorrhage;

Foetal distress is associated with forceps and big head only;

Surgical induction is associated with raised blood pressure and short first stage;

Raised blood pressure is associated with surgical induction;

Males associated with big head;

Greater maternal age is associated with forceps.

These relationships, occurring in all three weight groups, are shown more strikingly in Figure 3. It could be said Figure 3 illustrates how the outcome of a prolonged labour is likely to differ from one of normal length. From our present data we cannot offer any explanation

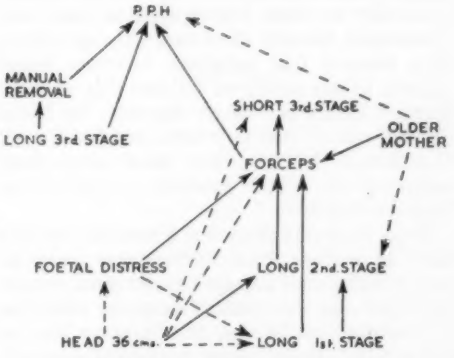



FIG. 3

Summary of relationships: primigravidae, 3,094 vertex presentations.

Factors related *regardless of weight of baby.*

*Key* ——→ related in all 3 groups, *significantly* in at least 2.

- - - -→ related in 2 groups, *significantly* in at least 1.

Where trends are contradictory they have been omitted.

*Note:* The analysis does not offer an explanation of the *long* 1st stage.

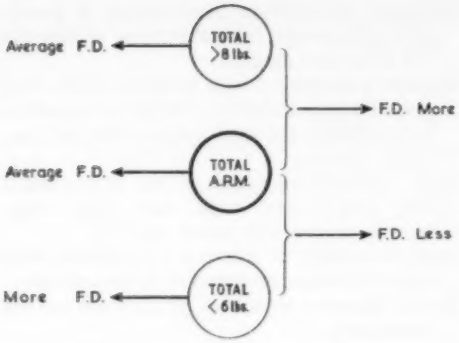



FIG. 4
Factors predisposing to foetal distress.

for the cause of the long labour, although large foetal head, irrespective of weight, is a suggestive factor; nor can we distinguish between the different types of long labour.

*Factor in Which Weight is Relevant*

An interesting fact emerges on considering surgical induction and foetal distress together. Previously we have been unable to show any relationship between these two, although others have claimed that induction increases foetal distress. In this survey we still find that when all induced babies are taken together the foetal distress rate is still very close to that for all non-induced labours; but subdividing them according to weight produces a change, as shown in Figure 4.

Thus, whereas babies over 8 pounds normally have an average foetal distress rate (note: in fact, it is *less* than average but not quite enough for 5 per cent significance) induction raises the rate to significantly *more* than average. On the other hand, those under 6 pounds normally have *more* foetal distress than any other weight group, but induction reduces the rate to *less* than average.

Since inductions are performed equally for postmaturity and pre-eclamptic toxaemia (40 per cent each) it is probable that the heavier group are postmature and the lighter group toxaemic. The indication for induction in 50 per cent of the lightest group is pre-eclampsia, a condition known to be hazardous for the foetus. It is therefore possible to deduce that induction for pre-eclampsia is effective in reducing these risks since the foetal distress rate in induced labours is 6 per cent and in non-induced over 12 per cent.

The converse seems to occur in the case of the heavier babies; 31 per cent of the induced group experiencing foetal distress compared with less than 18 per cent of the non-induced. If postmaturity is considered instead of weight the induced group has an even higher foetal distress rate, namely 60 per cent as compared with less than 20 in the non-induced. We hesitate to deduce that induction *causes* foetal distress in postmaturity: it is always possible that those suffering foetal distress have some additional complicating factor of which we have no record and further investigation of this point is needed.

## MULTIPARAE

*Length of First Stage*

Figure 5 illustrates the distribution of labours in the three weight groups.

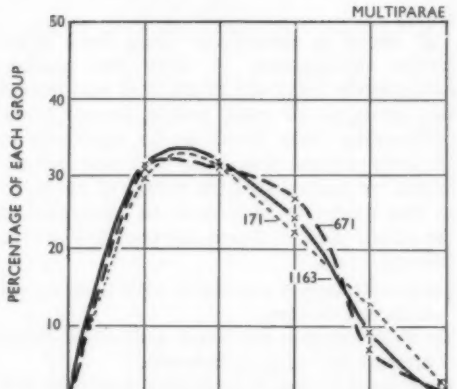



FIG. 5
Lengths of labour for three weight groups, multigravidae.

It will be seen that:

(1) There is great similarity between the 3 groups showing that in this as in other matters dealt with below, there is far greater homogeneity amongst multiparae than amongst primiparae.

(2) For large babies the mode is 6 hours and the average length of the first stage 11·2 hours. This group, 33·07 per cent, is, of course, relatively larger than it is for primiparae.

(3) For middle group, 58 per cent of multiparae, the mode is 7 hours and the average duration 10·9 hours.

(4) For small babies, 8·53 per cent, the mode is 7 hours and the average duration 12·1 hours.

In multiparae a labour lasting more than 20 hours seems to approximate to one of over 30 hours in a primiparous woman. Divided according to weight the percentage is as follows:

84·2 per cent of the first stages in the under 6 pounds (2,700 g.) group were completed before 20 hours.

88·9 per cent of the first stages in the 6–8 pounds group were completed before 20 hours.

89·8 per cent of the first stages in the over 8 pounds (3,600 g.) group were completed before 20 hours.

Or, 90 per cent of small babies were delivered by 25 hours, 90 per cent of average-sized babies by 21 hours and 90 per cent of large babies by 20 hours.

It would appear that it is the small baby which makes for difficulty—an exact reversal of the situation with primiparae but these differences are not quite significant at the 5 per cent level, however suggestive they may be; more cases are needed to substantiate the conclusion. We might assume that since birth weight increases with parity (Karn and Penrose, 1951) the very fact of a multiparous woman having a baby weighing less than 6 pounds (2,700 g.) is itself abnormal and one should therefore not be surprised that the labour also is abnormal. Is this effect found in each parity? Table I shows that with the second, third and fourth pregnancy the mean length of first stage is greatest where the child is underweight: after that the reverse is suggested but numbers are too small to be conclusive.

*Effect of Baby's Weight Upon Factors Other than Length of First Stage*

Table III (Part II) shows that in most factors there is very little deviation from the mean in multiparae. As in primiparae weight of baby is not significantly correlated with age of mother and length of third stage, nor in this case, with the forceps rate. The correlation between greater weight and longer second stage, greater post-partum haemorrhage, fewer stillbirths and more males is the same as for primiparae.

A multiparae's version of Figure 2 is impossible because of the remarkable shortage of deviations from the mean, but a few relationships unaffected by baby's weight are apparent:

Long first stage is associated with long second stage;

Short second stage is associated with small head;

Long third stage is associated with manual removal of placenta and post-partum haemorrhage;

Greater maternal age is associated with raised blood pressure, surgical induction and long second stage.

In the following, weight does make a difference:

Short first stage is associated with surgical induction if the baby is over 6 pounds.

## Discussion

It has been shown how in primiparae the forceps, foetal distress and stillbirth rates, the amount of post-partum haemorrhage and the length of the first and second stages differ in each of the three weight groups, greater weight apparently being disadvantageous in all these factors, except foetal distress and stillbirths where the reverse is true. It has also been pointed out that these differences are not necessarily *caused* by weight; by discovering which factors are similarly related to each other in each weight group we have been able to show that weight in itself is not the cause of a long second stage or of forceps or of post-partum haemorrhage, but that all these factors are more likely to follow a long first stage than a short one. As there are a greater number of long labours amongst big babies it follows that these undesirable factors are more common in this

group but it must also be borne in mind that as much as 85 per cent of large babies is delivered after labours of normal lengths and that long first stages are by no means absent in the other two groups; it is therefore not true to say that "a big baby means a long labour". This seems to bear out the opinion of Calkins (1955) and others that the weight of the baby is immaterial in determining the length of the first stage, providing there is no disproportion. The figures suggest that the size of the baby's head may be of far greater importance than its weight and incidentally, our finding that in the delivery of twins the first stage is short is relevant to this.

The same conditions appear in multiparae, with the great exception that increased foetal weight does not affect the length of the first stage; it is suggested that the baby's being underweight may be the cause of delay.

## Summary

(1) Over 5,000 cases of occipito-anterior presentations delivered vaginally have been analyzed to determine the effect of the baby's weight upon the length of the first stage of labour.

(2) In primiparae the first stage is longer where the baby is big but most labours fall within normal limits; in multiparae weight has no proven effect although it is suggested that the underweight baby is associated with the longer labour.

(3) It is also found that greater weight of baby is not in itself responsible for increased rates for forceps, post-partum haemorrhage or long second stage, but that these are likely consequences of the long first stage in all weight groups. No explanation is offered for the cause of the long first stage except that size of head is much more suggestive than weight and worthy of further investigation.

(4) It is found that it is the underweight baby which will probably suffer distress or die in labour.

Only trends which are similar in all three weight groups are included. Solid lines indicate factors which are significantly related at the 5 per cent level in 2 of the 3 weight groups. Dotted lines indicate factors in which the trend is again the same in all three groups but is significant in only one: the usual reason for lack of statistically significant relationships is smallness of numbers in the "under 6 pounds" group; these are not mentioned in the preceding list. The arrows could equally well point in the opposite direction, of course.

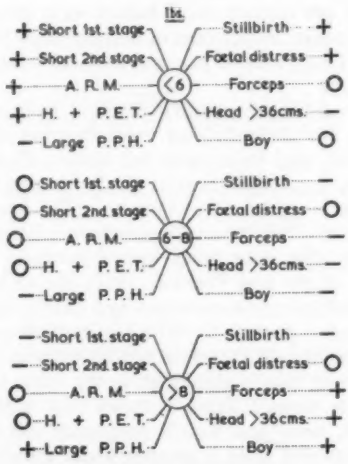
## Conclusions

(1) If a first stage is long it is more likely to be followed by a long second stage and by forceps, resulting in a short third stage (obstetric practice) and increased post-partum haemorrhage.

(2) An older mother is more likely to need forceps, which again ties up with the long second stage and increased post-partum haemorrhage.

(3) A large foetal head, irrespective of weight, produces a long second stage; it also seems to result in a long first stage if the baby is under 8 pounds (3,600 g.); again to be followed by forceps and short third stage.

Table IId




+ or − denotes significant relationships.
O denotes absence of significant relationship.

(4) Foetal distress often results in forceps and a short third stage, and in a baby of less than 8 pounds is associated with a long first stage.

(5) On the other hand, a long third stage—which we are unable to relate to length of the preceding labour in any way—will obviously end in manual removal with resultant increased haemorrhage. Thus we have a paradox, increased haemorrhage being preceded by either a long or a short third stage! Of course this occurs only in the special circumstances of forceps or manual removal; when the second and third stage proceeds normally there is close correlation between increasing length of third stage and increase in haemorrhage.

The conclusions are summarized in Table IId.

# FOETAL WEIGHT, PRESENTATION AND THE PROGRESS OF LABOUR

## Part II—Breech and Occipito-posterior Presentation Related to the Baby's Weight and the Length of the First Stage of Labour

BY

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### INTRODUCTION

IN our previous paper we presented the results of an investigation into the influence upon labour, especially the length of the first stage, of the baby's weight, with occipito-anterior presentations. Smallness of numbers precludes a detailed study of abnormal presentations but, finding that not only does the length of the first stage differ from the average but also that the average weight of such babies is markedly different, we shall try to show that it may well be the difference in weight and not the presentation which influences the duration of labour. Tables IIIa, b, and c show the results of the analysis.

TABLE IIIa

| | Primiparae | | | | Multiparae | | | |
|---|---|---|---|---|---|---|---|---|
| | All Patients | Vertex | Breech | Occiput-Posterior | All Patients | Vertex | Breech | Occiput-Posterior |
| 1st Stage: | | % | % | % | | % | % | % |
| Over 80 hours .. | 0·25 | 0·16 | 2* | 2* | 0·24 | 0·25 | 0* | 0* |
| 80— .. .. | 5·83 | 5·68 | 3* | 12+ | 2·01 | 1·97 | 3* | 3* |
| 40— .. .. | 19·51 | 19·51 | 14 | 23 | 8·95 | 8·97 | 6* | 10 |
| 20— .. .. | 35·61 | 35·63 | 26 | 41 | 25·22 | 25·15 | 23 | 28 |
| 10— .. .. | 26·81 | 27·0 | 30 | 18— | 31·82 | 32·0 | 43 | 21— |
| 5— .. .. | 11·99 | 11·95 | 26+ | 4— | 31·77 | 31·65 | 26 | 38 |
| 2nd Stage: | | | | | | | | |
| 2+ hours .. | 6·62 | 5·98 | 6* | 27+ | 0·67 | 0·5 | 9* | 1* |
| 2— .. .. | 39·96 | 39·73 | 41 | 46 | 7·8 | 7·4 | 14* | 16+ |
| ¾ .. .. | 46·28 | 47·06 | 41 | 25— | 44·79 | 44·91 | 27— | 45 |
| ½ .. .. | 7·12 | 7·17 | 12* | 2— | 46·75 | 47·17 | 40 | 38 |
| 3rd Stage: | | | | | | | | |
| 1+ hours .. | 2·12 | 2·16 | 0* | 2* | 1·96 | 2·07 | 0* | 1* |
| 1— .. .. | 1·75 | 1·74 | 3* | 1* | 1·29 | 1·31 | 3* | 0* |
| ½— .. .. | 4·36 | 4·49 | 0* | 3* | 4·74 | 4·69 | 6* | 6* |
| ¼— .. .. | 91·76 | 91·54 | 97+ | 94 | 91·97 | 91·93 | 91 | 93 |
| | | | Abnormal Presentations | | | | | |

+ or — denotes significant relationship at 5 per cent level.
* denotes too few patients for statistical analysis.

TABLE IIIb

| | Primigravidae | | | | Multigravidae | | | |
|---|---|---|---|---|---|---|---|---|
| | All Patients | Vertex | Breech | Occiput-Posterior | All Patients | Vertex | Breech | Occiput-Posterior |
| Age: | | | | | | | | |
| 40+ .. .. .. | 0·58 | 0·61 | 0* | 0* | 4·2 | 4·08 | 6* | 7* |
| 40— .. .. .. | 3·28 | 3·33 | 5* | 1* | 11·72 | 11·74 | 17* | 9 |
| 35— .. .. .. | 11·99 | 11·89 | 12 | 15 | 27·99 | 28·03 | 26 | 28 |
| 30— .. .. .. | 33·64 | 33·5 | 27 | 42 | 33·16 | 33·42 | 20 | 31 |
| 25— .. .. .. | 41·44 | 41·51 | 43 | 38 | 20·91 | 20·75 | 26 | 25 |
| 20— .. .. .. | 9·05 | 9·11 | 14 | 4 | 2·01 | 2·0 | 6* | 0* |
| Abnormal Presentations | | | | | | | | |

\+ or — denotes significant relationships at 5 per cent level.
* denotes too few patients for statistical analysis.

TABLE IIIc

| | Primigravidae | | | | Multigravidae | | | |
|---|---|---|---|---|---|---|---|---|
| | All Patients | Vertex | Breech | Occiput-Posterior | All Patients | Vertex | Breech | Occiput-Posterior |
| Post-partum haemorrhage: | | | | | | | | |
| 20+ ounces .. | 3·28 | 3·2 | 5* | 5* | 3·73 | 3·54 | 6* | 7 |
| 19— ounces .. | 14·75 | 14·34 | 20 | 24+ | 14·74 | 18·01 | 11* | 10 |
| 10— ounces .. | 81·95 | 82·4 | 76 | 71— | 81·54 | 81·45 | 83 | 83 |
| Surgical induction .. | 10·21 | 11·3 | 6* | 10 | 13·4 | 13·41 | 14* | 13 |
| Forceps .. .. | 8·34 | 5·88 | 73* | 42+ | 2·15 | 1·31 | 37* | 9* |
| Manual removal .. | 3·16 | 3·0 | 12+ | 3* | 2·63 | 2·67 | 3* | 1+ |
| Foetal distress .. .. | 8·73 | 8·08 | 12 | 20+ | 4·88 | 4·49 | 26+ | 6* |
| Stillbirths .. .. | 1·41 | 1·29 | 6* | 2* | 1·53 | 1·11 | 20 | 4 |
| Weight: | | | | | | | | |
| Over 8 pounds .. | 22·48 | 22·58 | 11— | 27 | 38·73 | 33·82 | 14— | 41 |
| 6–8 pounds .. | 68·18 | 68·38 | 60 | 66 | 57·8 | 58·62 | 29 | 49 |
| Under 6 pounds .. | 9·32 | 8·98 | 29+ | 7 | 8·47 | 7·56 | 57* | 10 |
| Head circumference: | | | | | | | | |
| Over 36 cm. .. | 17·6 | 17·47 | 20 | 14 | 20·29 | 20·66 | 11 | 14 |
| Under 36 cm. .. | 82·38 | 82·27 | 80 | 86 | 80·2 | 79·33 | 89 | 86 |
| Abnormal Presentations | | | | | | | | |

\+ or — denotes significant relationship at 5 per cent level.
* denotes too few patients for statistical analysis.

### Weight of Babies, Breech and Occipito-Posterior

The weight of babies presenting by the breech is significantly less than average. This occurs even though twins are excluded and although it is not the practice in this hospital to induce labour before term in breech presentations. In attempting to ascertain the effect of this presentation upon the duration of the first stage it is therefore of greater value to make the comparison with normally presenting babies which are smaller than average and not with the average.

The figures also suggest that babies with occipito-posterior may be larger than average but the difference just fails to reach significance at the 5 per cent level. Further investigation is necessary here.

### Primiparae

The effect of presentation upon the first stage of labour is shown in Figure 6: breech deliveries are shorter than average and occipito-posterior longer than average, the differences being significant at the 5 per cent level.

The percentage which reaches the second stage by 30 hours is 92 and 78 respectively, compared with 88·4 per cent of all occipito-anterior presentations. Ninety per cent of breech first stages are completed by 27 hours, while for occipito-posterior this took 47 hours, compared with 32 hours for normal vertex presentations.

### Breech

(i) *Length of the First Stage*

As we found, however, that babies delivered by the breech are significantly smaller than average, it would be more realistic to compare them with vertex (occipito-anterior) presentations weighing less than 6 pounds. This is done in Figure 7.

Here there is a much closer correlation. Thus in a breech delivery the first stage approximates most closely to the shortest vertex labour, the average duration being 14·2 hours compared with 16·3. It is even possible that the first stage

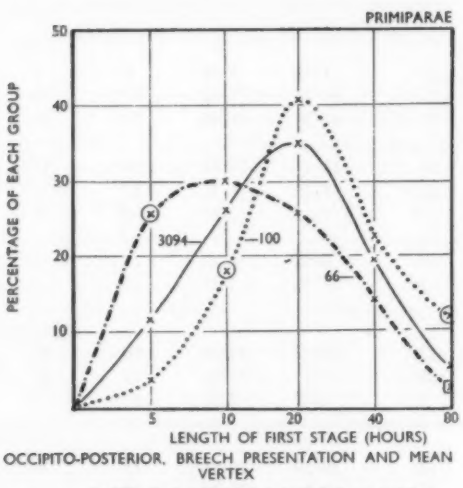



Fig. 6

Length of labour for abnormal presentations, primigravidae. (Note the code to figure is given in Part I, Figure 2.)

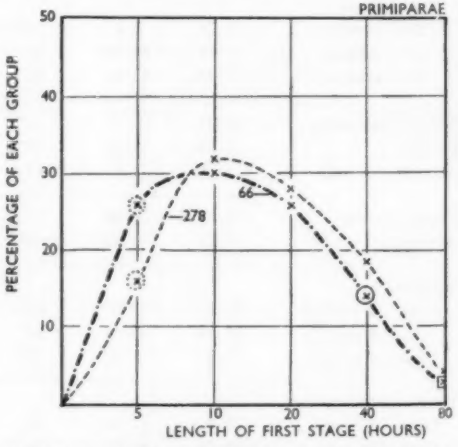



Fig. 7

Length of first stage of labour for breech presentations, primiparae.

is the shortest of all in breech deliveries but more cases are needed to confirm this suggestion.

Where the baby is large, however, delay occurs; the average duration of the first stage is 21 hours where the babies weigh over 8 pounds (3,600 g.), 14 hours where they weigh from 6 to 8 pounds and 10 where they weigh less than 6 pounds (2,700 g.). It is fortunate that they are usually of less than average weight.

(ii) *Other Factors*

A lengthening of the second stage might be expected but does not occur. The foetal distress and stillbirths rates are raised. The high forceps rate, 73 per cent (failed forceps are, of course, automatically excluded) may account for the short third stage (cf. Table IIIc) as well as the suggested greater post-partum haemorrhage and more manual removal. There is no correlation between breech presentation and size of foetal head, mother's age and surgical induction.

### Occipito-Posterior

(i) *Length of First Stage*

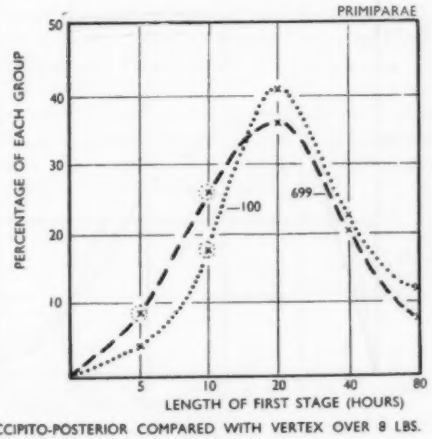
The closest correlation is with the group of babies presenting normally which weigh over 8 pounds, that is, with that group experiencing the longest first stages. This is to be expected, as our figures suggest a tendency for these babies to be heavier than average. It is shown that in this presentation the first stage is even longer, the average duration being 22·7 hours compared with 19·3. The fact that the mode is the same suggests that it is the increase in the number of prolonged labours which causes this increase in the average.

(ii) *Other Factors*

As one would expect, the second stage is longer than with the normal vertex, the forceps rate is higher (42 per cent compared with about 10 per cent in the largest and 6 per cent in the average occipito-anterior) and post-partum haemorrhage is slightly increased, perhaps in consequence. The foetal distress rate is also higher, the incidence being 20 per cent against about 6 per cent of the largest and 8 per cent of average sized occipito-anterior babies.

### Multiparae

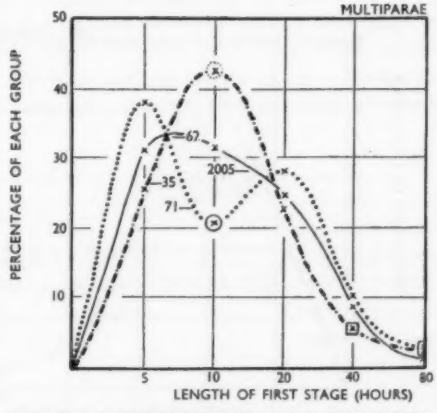
Although in most factors there is the lack of deviation from the average which seems to be




OCCIPITO-POSTERIOR COMPARED WITH VERTEX OVER 8 LBS.

FIG. 8

Length of first stage of labour occiput-posterior presentations, primiparae.




COMPARISON OF OCCIPITO-POSTERIOR, BREECH PRESENTATION AND VERTEX (MEAN)

FIG. 9

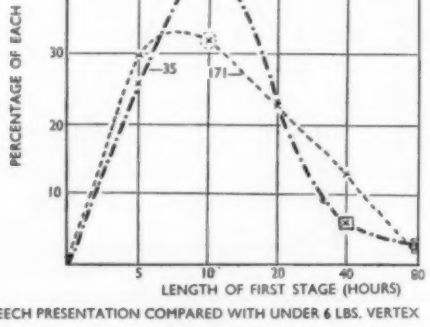
Length of first stage of labour, multiparae, abnormal presentations.

typical of the multiparous patient (see Table III) the length of the first stage is of unusual interest (see Fig. 9). The results are not as simple as those for primiparae although the same trend is followed, the percentage which reaches the second stage by 20 hours being 92 for breech, 87 for occipito-posterior and 88·8 for occipito-anterior presentations. Alternatively, we could say that 90 per cent of breech deliveries have completed the first stage by 18·5 hours, 90 per cent of occipito-posterior deliveries by 22·5 hours, compared with 21·5 hours for the average occipito-anterior.

### Breech

(i) *Length of First Stage*

Babies presenting by the breech are smaller than average, as in primiparae. It was found, however (Table IIa, Part I), that in the multiparous patient it was the small baby which was likely to be associated with longer labours; now we find that when the small baby is "turned upside down" long labour is much reduced and labour becomes normal (see Fig. 10). The average duration is shortened from 12·7 to 11·7 hours.




BREECH PRESENTATION COMPARED WITH UNDER 6 LBS. VERTEX

Fig. 10

Length of first stage of labour, breech presentations, multiparae.

(ii) *Other Factors*

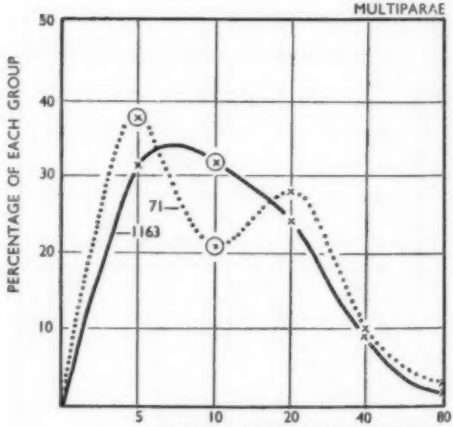
The foetal distress and stillbirth rates are greatly increased, long second stages are more common than with the normal vertex presentations and forceps were necessary in 37 per cent of the cases. Breech presentation does not seem to affect the length of the third stage, postpartum haemorrhage or manual removal.

### Occipito-Posterior

(i) *Length of the First Stage*

The fact that the curve for the first stage in occipito-posterior presentation is bi-modal (see Fig. 11) may indicate that for some multiparae this is the optimum presentation, since they have the shortest labours of all; but if a multiparous patient is not delivered very quickly she will linger longer than she would with a baby presenting normally.

There are two possible explanations of this rapid first stage: either (1) these are cases of anthropoid pelvis, which is said to predispose to this presentation, in which case occipito-posterior is the normal and not the abnormal




OCCIPITO-POSTERIOR COMPARED WITH VERTEX 6–8 LBS.

Fig. 11

Length of first stage of labour, occiput-posterior, multiparae.

presentation; or (2) the rapid first stages may be in the delivery of the smaller babies:

| | Over 8 Pounds (3,600 g.) | 6–8 Pounds | Under 6 Pounds (2,700 g.) |
|---|---|---|---|
| Average length of first stage (hours): | | | |
| Occipito-anterior .. .. | 11·2 | 10·9 | 12·1 |
| Occipito-posterior .. | 15·9 | 9·0 | 8·2 |

These figures show that while in normal presentations delay occurs with the small babies, in occipito-posterior presentation it occurs with the larger ones.

(ii) *Other Factors*

Other factors are related to this presentation as in multiparae, namely, slightly longer second stage, more forceps and more post-partum haemorrhage.

## Discussion

### *Effect of Weight Upon Duration of the First Stage*

In primiparae the duration of the first stage of labour with abnormal presentation is very like that with a normal vertex presentation of the similar weight. In multiparae the situation is more complicated but an abnormal presentation is by no means a disadvantage, as far as length of the first stage is concerned.

Although the number of cases is very small and the conclusions reached can only be tentative, it is interesting to glance at the average length of the first stage in each weight group as shown in the following table:

*Average Duration of First Stage (Hours)*

| | Over 8 Pounds (3,600 g.) | 6–8 Pounds | Under 6 Pounds (2,700 g.) |
|---|---|---|---|
| Primiparae: | | | |
| Normal vertex .. .. | 18·6 | 16·9 | 15·6 |
| Breech .. .. .. | 20·7 | 15·0 | 10·1 |
| Occipito-posterior .. | 27·3 | 22·8 | 18·2 |
| Multiparae: | | | |
| Normal vertex .. .. | 11·2 | 10·9 | 12·1 |
| Breech .. .. .. | 8·5 | 10·5 | 10·95 |
| Occipito-posterior .. | 15·9 | 9·0 | 8·2 |

Thus, in primiparae, the average duration of the first stage is longer with a larger baby, in every presentation. With occipito-posterior labour is long in every weight group; with breech labour is shorter where the baby weighs less than 8 pounds (3,600 g.) but is delayed when it is larger.

In multiparae, normal vertex and breech presentations are similar in that the smallest babies are associated with delay; with occipito-posterior the average duration increases with weight, but we have already noted a group in which this presentation is associated with the most rapid labour of all.

## Summary

(1) Babies presenting by the breech are smaller than average; those with occipito-posterior may be larger.

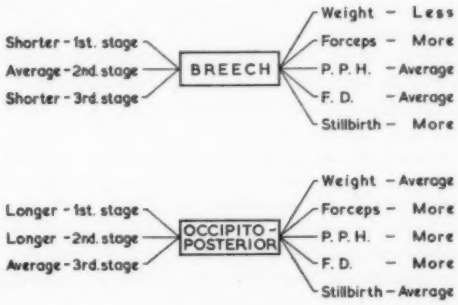
(2) In primiparae, the length of the first stage with breech presentation is shorter than for the average normal vertex; it resembles the first stage of the smallest occipito-anterior babies and may be even shorter than this, the shortest normal labour.

(3) With primiparae O.P. the first stage is longer than with the average normal vertex presentation; it resembles the first stage of the largest occipito-anterior babies and may be even longer than this, the longest normal labour.

(4) In multiparae breech labour resembles the average; it does not resemble that associated

Table IIId

PRIMIPARÆ



with the smallest occipito-anterior babies in spite of similarity of weight, because it is abnormal for the baby of a multiparous patient to weigh less than 6 pounds unless it is a breech.

(5) Labour with an occipito-posterior presentation in multigravidae is shorter than with all other types unless the foetus exceeds 8 pounds.

The conclusions are summarized in Table IIId.

## Acknowledgments

This work was undertaken as part of a programme of research made possible by the generosity of the Nuffield Foundation. We are very grateful to Professor L. S. Penrose of University College for advice and help, to the staff of the Obstetric Hospital, University College Hospital, and especially to Miss Ann Hart for invaluable assistance with punched cards and record-keeping.

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# AN IMMUNOCHEMICAL STUDY OF THE PROTEINS OF AMNIOTIC FLUID AND OF MATERNAL AND FOETAL SERUM

BY

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AND

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EXISTING information about amniotic fluid protein, based mainly on electrophoretic analysis, leaves considerable doubt about the nature and source of this protein. No quantitative data using the more precise immunochemical methods have been published. We therefore report an immunochemical study of this protein, which suggests that it arises from the maternal serum by ultrafiltration and also some data on the concentrations of seven serum proteins in maternal and foetal serum.

## METHODS

Amniotic fluid, maternal serum and foetal serum from fourteen normal pregnancies and five toxaemic pregnancies were examined.

Amniotic fluid from the hind waters was obtained by Drew-Smythe catheter from patients in whom labour was induced by rupture of the membranes for suspected disproportion or for suspected postmaturity (5–12 days) in otherwise normal pregnancies. Material from toxaemic patients was similarly obtained between the thirty-sixth and fortieth weeks of pregnancy. Maternal serum was obtained during the first two days after delivery. Cord blood was used as the source of foetal serum. The amniotic fluid was centrifuged at 13,000 r.p.m. for 30 minutes to get rid of cellular debris, lanugo, etc. The protein content of the amniotic fluid and sera was determined by the biuret method, and albumin, siderophilin, $\gamma$ globulin, ceruloplasmin, 19S component of $\gamma$ globulin (called $\beta_2$M by the French workers), $\alpha_2$ glycoprotein and $\beta$ lipoprotein were estimated by the immunological method of Gell (1957). This is a titration procedure with an end point depending on visual matching of the pattern of precipitate obtained by the unknown with that from a standard. The details of the modification of the method for study of concentration ratios in various biological fluids, the details of raising the antisera, and the calculation of the errors of the determinations are to be reported (J. F. Soothill, in preparation). The errors, which are slightly different for each protein, are dependent on the concentration of the protein present, and the coefficient of variation for the estimation of each protein is constant over a wide range of concentrations. Values obtained for the coefficients of variation, for the highest dilution at which the protein can be estimated in normal human serum and accepted values of molecular weights of these proteins, are given in Table I.

For each case, the amniotic fluid was titrated against the maternal and the foetal serum, on separate plates, thus obtaining amniotic fluid/serum concentration ratios for each protein by a direct reading for each of the sera, with the error of a single determination. In addition, a suitable dilution of standard serum from a healthy adult male was placed on each plate, so that estimates of the concentration of each protein in foetal and maternal serum could be obtained, expressed as a percentage of this standard. The standard serum is known to be normal for all these proteins. The ranges of

TABLE I

| Protein | Albumin | Siderophilin | $\gamma$ Globulin | Cerulo-plasmin | $\alpha_2$ Glyco-protein | 19S$\gamma$ Globulin | $\beta$ Lipoprotein |
|---|---|---|---|---|---|---|---|
| Molecular weight .. | 68,000 | 90,000 | 150,000 | 150,000 | 840,000 | 900,000 | 1–3,000,000 |
| Coefficient of variation .. | 34 | 19 | 13 | 15 | 25 | 17 | 18 |
| Highest detectable dilution of serum | 1/32,448 | 1/2,048 | 1/16,224 | 1/256 | 1/1,024 | 1/64 | 1/256 |

Molecular weight, coefficient of variation of the estimation and highest dilution of serum at which the protein is still detectable for the seven serum proteins studied.

normality in healthy subjects expressed this way are to be reported elsewhere (J. F. Soothill, in preparation). Amniotic fluid from one case (number 6) was concentrated 25-fold by ultrafiltration (method of Grant, 1959) and estimates of the proteins not detected in the unconcentrated material ($\alpha_2$ glycoprotein, 19S component of $\gamma$ globulin and $\beta$ lipoprotein) were repeated.

Proteins from the amniotic fluid from three normal pregnancies were concentrated to 1 g./100 ml. and were injected into a rabbit, using four subcutaneous injections of a Freund's adjuvant preparation and intraperitoneal and intravenous injections of a saline solution (the details of the course are to be described elsewhere —J. F. Soothill) to produce a rabbit antiserum to human amniotic fluid proteins.

The antiserum was absorbed with equal volumes of human serum, at room temperature, for two hours and then at 4° C. for twenty-two hours. The precipitate was removed by centrifugation. The absorbed and the unabsorbed antisera were examined by immuno-electrophoresis (modified from Grabar and Williams, 1953).

## RESULTS

Table II shows the results obtained in fourteen normal pregnancies. Concentrations of seven proteins, in maternal and foetal serum, are expressed as a percentage of the standard serum of a healthy adult male. This standard should not be regarded as a precise indication of normality, as there is a range for each protein in a healthy population and the concentration of some proteins varies between the sexes (e.g., ceruloplasmin is higher in females), but it provides a satisfactory basis for comparison between the concentration of the proteins in maternal and foetal sera, and indicates the gross deviations from the non-pregnant adult state (e.g., the elevation of ceruloplasmin and siderophilin in the mother's sera). The concentration ratios for amniotic fluid/maternal serum and amniotic fluid/foetal serum are given for each protein. In addition, the total protein concentration of each specimen is given.

Normal maternal serum total protein concentration ranged from 4·6 to 6·9 g./100 ml., which is lower than that of normal non-pregnant women, and is consistent with previous studies (Coryell *et al.*, 1950; MacGillivray and Tovey, 1957). Albumin was lower than normal, and probably accounted for most of this difference in total protein concentration. Ceruloplasmin was grossly raised, as has been shown by Markowitz *et al.* (1955) and the elevation of siderophilin was in keeping with the known rise of iron-binding capacity in pregnancy (Fay *et al.*, 1949). (The estimation of siderophilin by this technique correlates precisely with the iron binding capacity (Neale and Soothill, to be published).) $\alpha_2$ glycoprotein, and the 19S component of $\gamma$ globulin appeared to be slightly, but not consistently, raised.

Foetal serum total protein concentrations were lower than the maternal sera. This is in keeping with the majority of previous publica-

TABLE II

| No. | Serum Protein Concentrations (% of Standard) | | | | | | | | | | | | | | | | Amniotic Fluid | Concentration Ratios | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | Maternal Serum | | | | | | | | Foetal Serum | | | | | | | | | Amniotic Fluid / Maternal Serum | | | | | Amniotic Fluid / Foetal Serum | | | | |
| | Total Protein g./100 ml. | A | S | γ | C | α | 19Sγ | β | Total Protein g./100 ml. | A | S | γ | C | α | 19Sγ | β | Total Protein mg./100 ml. | A | S | γ | C | α | A | S | γ | C | α |
| 1 | 6·6 | 100 | 400 | 100 | 400 | 200 | 200 | — | 5·7 | 125 | 175 | 175 | 62 | 100 | 50 | — | 510 | 1/28 | 1/16 | 1/64 | 1/64 | 0 | 1/32 | 1/10 | 1/80 | 1/16 | 0 |
| 2 | 5·3 | 50 | 200 | 50 | — | 200 | 200 | — | 4·3 | 50 | 87 | 75 | — | 100 | 37 | — | 250 | 1/20 | 1/28 | 1/128 | — | 0 | 1/32 | 1/12 | 1/128 | — | 0 |
| 3 | 6·0 | 50 | 150 | 150 | 350 | 200 | 150 | 150 | 5·1 | 50 | 62 | 150 | 75 | 100 | 25 | 25 | 360 | 1/20 | 1/16 | 1/64 | 1/96 | 0 | 1/16 | 1/8 | 1/80 | 1/20 | 0 |
| 4 | 6·4 | 62 | 200 | 200 | 250 | 100 | 150 | — | 6·1 | 80 | 100 | 175 | 75 | 100 | 37 | — | 254 | 1/24 | 1/24 | 1/144 | 1/80 | 0 | 1/32 | 1/16 | 1/128 | 1/24 | 0 |
| 5 | 5·7 | 75 | 150 | 100 | — | 100 | 150 | 100 | 5·6 | 100 | 87 | 125 | — | 75 | 25 | — | 300 | 1/20 | 1/12 | 1/64 | — | 0 | 1/32 | 1/8 | 1/64 | — | 0 |
| 6 | 6·5 | 50 | 600 | 125 | — | 150 | 125 | — | — | 62 | 75 | 100 | — | 50 | 37 | — | 336 | 1/12 | 1/16 | 1/64 | — | 0 | 1/10 | 1/4 | 1/56 | — | 0 |
| 7 | 4·6 | 62 | 200 | 50 | — | 100 | 200 | 150 | 5·9 | 100 | 87 | 125 | — | 100 | 50 | 25 | 170 | 1/64 | 1/56 | 1/64 | — | 0 | 1/64 | 1/28 | 1/192 | — | 0 |
| 8 | 5·7 | 62 | 300 | 62 | 250 | 150 | 200 | 150 | 5·4 | 87 | 125 | 100 | 75 | 100 | 75 | 22 | 240 | 1/16 | 1/24 | 1/32 | 1/64 | 0 | 1/16 | 1/14 | 1/64 | 1/16 | 0 |
| 9 | 5·6 | 75 | 250 | 75 | 400 | 400 | 175 | 125 | 5·2 | 62 | 75 | 50 | — | 87 | 16 | 37 | 240 | 1/32 | 1/56 | 1/128 | 1/128 | trace | 1/32 | 1/24 | 1/128 | — | trace |
| 10 | 5·5 | 75 | 150 | 62 | — | 62 | 100 | 150 | 4·9 | 62 | 75 | 150 | — | 100 | 12 | 25 | 265 | 1/32 | 1/32 | 1/64 | — | trace | 1/24 | 1/16 | 1/128 | — | trace |
| 11 | 6·8 | 62 | 125 | 87 | — | 250 | 150 | 87 | 5·2 | 75 | 75 | 75 | — | 100 | 12 | 15 | 260 | 1/32 | 1/48 | 1/112 | — | trace | 1/48 | 1/16 | 1/128 | — | trace |
| 12 | 6·9 | 100 | 175 | 125 | — | 200 | 200 | 125 | 6·1 | 125 | 125 | 150 | — | 200 | 43 | 37 | 285 | 1/40 | 1/32 | 1/112 | — | 0 | 1/48 | 1/28 | 1/128 | — | 0 |
| 13 | 5·4 | 50 | 100 | 62 | — | 50 | 150 | 125 | 5·4 | 62 | 87 | 62 | — | — | 25 | 12 | 298 | 1/16 | 1/20 | 1/32 | — | 1/512 | 1/32 | 1/16 | 1/56 | — | — |
| 14 | 6·1 | 50 | 125 | 62 | — | — | 250 | 87 | 5·4 | 50 | 100 | 62 | — | — | 37 | 12 | 177 | 1/24 | 1/32 | 1/56 | — | 0 | 1/20 | 1/20 | 1/56 | — | 0 |
| Mean | 5·9 | 66 | 223 | 94 | 330 | 166 | 171 | 125 | 5·4 | 78 | 90 | 112 | 72 | 101 | 34 | 23 | 282 | | | | | | | | | | |

Results obtained in fourteen normal pregnancies. Concentrations of seven serum proteins in maternal and foetal serum, expressed as a percentage of the standard "normal" serum, and concentration ratios for these proteins in amniotic fluid, related to maternal and to foetal sera. A = albumin, S = siderophilin, γ = γ globulin (7S or main component), C = ceruloplasmin, α = $\alpha_2$ glycoprotein, 19Sγ = 19 S component of γ globulin, β = β lipoprotein. Where material was insufficient for the determination a dash (—) is given. No 19Sγ globulin or β lipoprotein was detected in amniotic fluid. Where other proteins were not detected, a zero (0) is given.

tions (Moore *et al.*, 1949; Abbas and Tovey, 1960) but differs from Brown *et al.* (1959), who found the same concentration as in the maternal serum. The mean of our albumin values from foetal sera was greater than that for maternal sera, but was lower than that for normal adults, and consistent with the electrophoretic results of Brown *et al.* (1959) and Longsworth *et al.* (1945), but the error of our determination is such that our results on this protein are relatively crude compared with electrophoresis. The mean of the foetal serum $\gamma$ globulin was higher than that for maternal serum, in keeping with the findings of Brown *et al.* (1959). $\alpha_2$ glycoprotein in the foetal serum was similar in concentration to that in normal adults.

The concentrations of the other proteins studied differed strikingly from the maternal serum. $\beta$ lipoprotein, 19S $\gamma$ globulin, ceruloplasmin and siderophilin were all present in much lower concentrations than in maternal serum (in which all but $\beta$ lipoprotein are raised as compared with normal adult serum) and are lower than in normal adult serum, with the possible exception of siderophilin. Hitzig (1957), using the less sensitive and non-quantitative technique of immunoelectrophoresis, failed to detect $\beta_2$M (identical with 19S $\gamma$ globulin) in newborn infants' serum. The discrepancy is probably due to the greater sensitivity of our technique.

The four smaller serum proteins were all detected in the amniotic fluid. Albumin and siderophilin were present in the greatest proportion of their concentration in serum. $\gamma$ globulin and ceruloplasmin were present in a smaller proportion and $\beta$ lipoprotein and the $S_{19}$ component of $\gamma$ globulin were not found. $\alpha_2$ glycoprotein (also 19S by ultracentrifugal analysis) could just be detected in some amniotic fluids; by concentrating the amniotic fluid 25-fold in Case 6, in which it had not been found, it was shown to be present in 1/800 of the amount present in the maternal serum. The 19S component of $\gamma$ globulin is present in serum in much lower concentration than $\alpha_2$ glycoprotein, and would therefore be only just detectable at this concentration, if the concentration ratio was the same as that of $\alpha_2$ glycoprotein, but, in fact, none was found. $\beta$ lipoprotein was also not detected showing that if it is present at all, the concentration ratio was considerably less than 1/800. Thus the relative concentrations of these proteins, selected as they are to provide a wide range of molecular size, suggest that serum proteins enter the amniotic fluid by a process of selective ultrafiltration from serum.

Table I includes three pairs of proteins of rather similar molecular weights—albumin and siderophilin, $\gamma$ globulin and ceruloplasmin, and $\alpha_2$ glycoprotein and 19S $\gamma$ globulin. In each of these pairs, there is one protein of widely different concentration in maternal and foetal serum. It would be expected that the proteins in each of these pairs would be ultrafiltered at about the same rate, so that the concentration ratio of amniotic fluid to serum from which they arose should be the same. Unfortunately 19S $\gamma$ globulin is not detectable in amniotic fluid, so

TABLE III

| | Siderophilin / Albumin % | | Ceruloplasmin / $\gamma$ % | |
|---|---|---|---|---|
| | Maternal | Foetal | Maternal | Foetal |
| | 175 | 310 | 100 | 500 |
| | 71 | 270 | 70 | 400 |
| | 125 | 200 | 200 | 530 |
| | 100 | 200 | 50 | 400 |
| | 166 | 400 | 50 | |
| | 80 | 250 | | |
| | 114 | 225 | | |
| | 67 | 112 | | |
| | 67 | 150 | | |
| | 100 | 150 | | |
| | 67 | 300 | | |
| | 80 | 170 | | |
| | 80 | 200 | | |
| | 67 | 100 | | |
| Mean .. .. | 97·07 | 217·93 | 94 | 457·5 |
| Number of comparisons (n) | 14 | 14 | 5 | 4 |
| Standard error of mean .. | 9·7 | 22·2 | 28·0 | 33·8 |
| Difference from 100 .. | 2·93 | 117·93 | 6 | 357·5 |
| $t_{(n-1)}$ .. .. | 0·30 | 5·32 | 0·21 | 10·58 |
| P .. .. | >0·7 | <0·001 | >0·8 | <0·01 |

Amniotic fluid/serum concentration ratios for maternal and foetal serum, of siderophilin, expressed as a percentage of the ratio of albumin, and that of ceruloplasmin, expressed as a percentage of that of $\gamma$ globulin. In each case the ratio for maternal serum did not differ significantly from 100 per cent, whereas the ratio for foetal serum did.

the ratio of this protein to $\alpha_2$ glycoprotein cannot be studied, but the other two pairs give valid comparison. In Table III the amniotic fluid/serum concentration ratios for both maternal and foetal sera, of siderophilin, are expressed as a percentage of those of albumin, and the ratios for ceruloplasmin are expressed as a percentage of those of $\gamma$ globulin. It will be seen that in both the pairs of proteins, the relative concentrations in amniotic fluid agree well with those in maternal serum, but differ from those of foetal serum. This strongly suggests that the amniotic fluid protein is an ultrafiltrate of maternal serum, and not of foetal serum.

Results of similar determinations made on five patients with pregnancy complicated by moderately severe pre-eclamptic toxaemia are shown in Table IV. They revealed no consistent difference from those from normal pregnancies, other than the depression of the maternal albumin in Case 1, which presumably resulted from the proteinuria.

The anti-amniotic fluid antiserum produced a number of lines of precipitation when reacted with amniotic fluid protein and with serum by immunoelectrophoresis. After absorption of the antiserum with normal human serum, no lines of precipitate were obtained on immunoelectrophoresis with amniotic fluid protein. Thus no evidence was obtained of proteins other than serum proteins in the amniotic fluid.

## Discussion

Several different sources have been suggested for the origin of the proteins in amniotic fluid, as a result of analysis of this protein by different techniques. Earlier workers (Zangemeister and Meissl, 1903; Makepeace *et al.*, 1931; Cantarow *et al.*, 1933), considered amniotic fluid to be a dialysate of serum mixed with foetal urine, but did not say whether the serum was foetal or maternal. In a study of many constituents of amniotic fluid, including paper electrophoresis of the protein, Palliez *et al.* (1956) came to the conclusion that amniotic fluid was not a dialysate of serum, but the product of secretion of the amniotic epithelium; this conclusion was based largely on the study of the non-protein constituents. Barbanti (1956), McKay, Richardson and Hertig (1958) and Abbas and Tovey (1960) concluded from paper electrophoretic analysis of the proteins of amniotic fluid that they arose by filtration of maternal serum through a semipermeable membrane. Abbas and Tovey demonstrated such filtration *in vitro* through foetal membranes (amnion and chorion). On the other hand, Mentasti (1959), using a method of free microelectrophoresis, obtained different results from those obtained by paper electrophoresis. He concluded that the protein pattern of amniotic fluid bore more resemblance to that of foetal serum than to that of maternal serum.

Even if Palliez *et al.* (1957) were right in their conclusion that some of the non-protein constituents of amniotic fluid arose by a process more complicated than simple dialysis, there is no reason to extend this deduction to the protein constituents and the simple hypothesis of filtration through a semipermeable membrane must still be considered as the origin of the proteins. If the amniotic fluid/serum concentration ratios for serum proteins are inversely in the order of their molecular size (that is, if there is preferential selectivity for the smaller proteins) such a simple filtration mechanism would be likely.

Electrophoretic fractions of serum proteins other than the albumin and $\gamma$ globulin fractions, are such complex mixtures of proteins of widely differing molecular size (Grabar and Burtin, 1960), that data obtained by electrophoresis is of very limited value in assessing the possibility of ultrafiltration as a source of this protein. Immunochemical techniques estimate individual proteins, which are homogeneous for molecular size, and are therefore much more applicable to this type of problem.

The failure to obtain antibodies to non-serum proteins when a rabbit was immunized with concentrated amniotic fluid protein suggests, though it does not prove, that the protein of amniotic fluid is at least vastly predominantly composed of serum proteins. The quantitative data show that albumin, $\gamma$ globulin and siderophilin account for most of it. The relative concentrations of the proteins strongly suggest that the protein arises as an ultrafiltrate of maternal serum.

In interpreting such results, however, the probability must be borne in mind that the

TABLE IV

| No. | Serum Protein Concentrations (% of Standard) | | | | | | | | | | | | | | | Amniotic Fluid | Concentration Ratios | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | Maternal Serum | | | | | | | | Foetal Serum | | | | | | | | Amniotic Fluid / Maternal Serum | | | | | Amniotic Fluid / Foetal Serum | | | | |
| | Total Protein g./100 ml. | A | S | γ | C | α | 19Sγ | β | Total Protein g./100 ml. | A | S | γ | C | α | 19Sγ | β | Total Protein mg./100 ml. | A | S | γ | C | α | A | S | γ | C | α |
| 1 | 5·5 | 37 | 125 | 37 | 300 | 150 | 200 | — | 5·8 | 62 | 200 | 75 | 75 | 100 | 12 | — | 304 | 1/10 | 1/12 | 1/48 | 1/48 | 1/512 | 1/14 | 1/12 | 1/56 | 1/8 | trace |
| 2 | 5·8 | 75 | 200 | 50 | — | 100 | 150 | — | 6·2 | 100 | 150 | 75 | — | 50 | 37 | — | 186 | 1/64 | — | 1/128 | — | 0 | 1/96 | 1/24 | 1/384 | — | 0 |
| 3 | 6·4 | 75 | 100 | 125 | — | 200 | 175 | 100 | 7·3 | 87 | 87 | 87 | — | 50 | 37 | 25 | 390 | 1/8 | 1/12 | 1/64 | — | 0 | 1/12 | 1/8 | 1/128 | — | 0 |
| 4 | 6·6 | 62 | 250 | 100 | — | 150 | 150 | — | 5·2 | 87 | 150 | 100 | — | 150 | 25 | — | 275 | 1/40 | 1/24 | 1/64 | — | 0 | 1/48 | 1/16 | 1/64 | — | 0 |
| 5 | 5·3 | 50 | 150 | 62 | — | 100 | 200 | 87 | 5·3 | 62 | 125 | 100 | — | 100 | 37 | 22 | 197 | 1/16 | 1/24 | 1/64 | — | 0 | 1/24 | 1/28 | 1/80 | — | 0 |
| Mean | 5·9 | 60 | 165 | 75 | — | 140 | 160 | | 6·0 | 80 | 142 | 87 | | 90 | 30 | | 270 | | | | | | | | | | |

Results obtained in 5 pregnancies complicated by pre-eclamptic toxaemia. Results are expressed similarly to those in Table I.

proteins are in dynamic equilibrium, with continuous filtration and reabsorption. One likely route of disappearance from the amniotic fluid is drinking by the foetus, when the protein is, no doubt, digested and absorbed. This process would be non-selective for the different proteins and so would not affect the interpretation of our results. The possibility of other selective disappearance remains, but appears unlikely.

There was no consistent evidence to suggest that the amniotic membranes in patients with pre-eclamptic toxaemia are abnormally permeable to proteins as are the filtration membranes in the glomeruli of the kidneys.

It was not the aim of the present research to elucidate the more complex problem of the origin of foetal serum proteins, and their relationship to the maternal serum proteins. Transmission of serum proteins across the placenta certainly occurs, in view of the presence of maternal antibodies in foetal serum, and is likely to be in some degree selective according to molecular weights. The rate of foetal production may well differ for different proteins relative to the adult and possibly the rate of utilization may also differ. In Table II it will be seen that albumin and $\gamma$ globulin are present in the foetal serum at slightly higher concentration (dehydration may account for this). The other proteins are in much lower concentration, and, if placental transfer is the main source, the larger molecular size of $\alpha_2$ glycoprotein, 19S $\gamma$, and $\beta$ lipoprotein could account for this, but the relatively low concentration of siderophilin and ceruloplasmin in the foetus remains unexplained by any such filtration mechanism. The high concentration of $\gamma$ globulin is consistent with the observation of Bangham (1960) that this protein is selectively transmitted into the foetal serum in the rhesus monkey; he also showed that the $\gamma$ globulin in rhesus monkey amniotic fluid arose from the maternal serum, and not from the foetus.

## Summary

(1) Quantitative immunochemical study of the protein of amniotic fluid suggests that it arises by selective ultrafiltration from the maternal serum, and not from the foetal serum. There was no evidence of non-serum amniotic fluid protein.

(2) Serum concentrations for seven proteins in maternal and foetal serum are reported. The elevation of siderophilin and ceruloplasmin in maternal serum is confirmed. 19S component of $\gamma$ globulin was present in foetal serum at low concentration.

(3) Amniotic fluid protein in pregnancy complicated by toxaemia did not differ consistently from that of normal pregnancy.

## Acknowledgments

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# MÜLLEROMA—A RARE CAUSE OF DYSMENORRHOEA

BY

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FOUR cases of extremely severe dysmenorrhoea in young girls aged from 18–24 years were described by Conill Serra (1950). Conservative treatment had failed to produce any relief and in one case even a laparotomy, with metrotomy and pre-sacral neurectomy, had not helped. In all cases a small tumour was found in relation to the uterine end of the round ligament, or the uterine cornu, and removal of these produced complete relief from symptoms. In a subsequent paper Conill (1954) described a fifth case in which the findings were similar and in which also removal of the tumour produced complete and permanent relief of symptoms.

In each instance the tumour was quite small with a diameter of about 2–3 cm. and showed a thick, muscular coat with a small central cavity containing blood. The cavity was lined by a cylindrical epithelium like that of a miniature uterus. It has been suggested that the mass represents an atretic supplementary uterus derived either from an accessory Müllerian duct, or by abnormal localization under the influence of the gubernaculum of Hunter of a small part of the duct about the twelfth week of intra-uterine life. Conill (1954) has suggested the term "Mülleroma" for this tumour in view of its supposed origin.

In no case of the above series was any lesion found other than the small swelling which was removed and it is considered that this is a separate entity, quite distinct from adenomyoma, endometriosis, rudimentary atretic uterine horn, and pelvic inflammation. Adenomyoma does not present a single central cavity surrounded by a muscular wall as seen in these cases. Endometriosis may be found in the situation of these tumours, but again does not show the same arrangement of stroma in relation to the glandular elements of the ectopic endometrium. A rudimentary uterine horn can be distinguished because it gives origin to the round ligament, tube and ovarian ligament and has a more or less permeable connection with the hemi-uterus of the opposite side. No evidence of any of these was found in relation to the tumours in question. No evidence of inflammation was observed in any of the cases recorded.

The following cases are presented since I have found no reference in the British literature to anything of the kind and because they seem to conform to the description of Mülleroma as described by Conill Serra (1950) and Conill (1954). I have recently had the opportunity of discussing the diagnosis in the first case with these authors and they have confirmed that its features place it in the same category as their own cases.

*Case 1*

L.M.P., aged 20 years, was first seen in 1953, complaining of pain in the left iliac fossa which had been present, off and on, for a few months. Menstruation had begun at the age of 13 and the cycle had been regular, 7/28, with relatively little pain until a few months before she reported. The only positive finding at this time was a loaded colon which was rather tender, and treatment with laxatives was instituted. This, however, failed to prevent increasingly severe pain and almost two years later she was sent into hospital as an emergency with severe left-sided pelvic pain, associated with a period which had begun a few days previously. By this time she was incapacitated by the pain for about three days each month and had to take to her bed. In the intervals between her periods, she

FIG. 1
Case 1. Mülleroma. ×2·39.

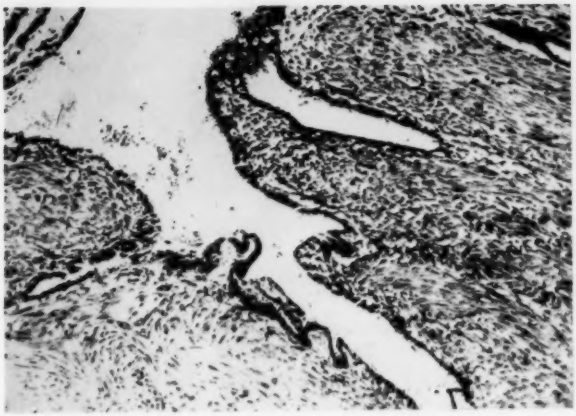

FIG. 2
Case 1. Section of Mülleroma showing endometrial stroma and columnar epithelium. ×86.

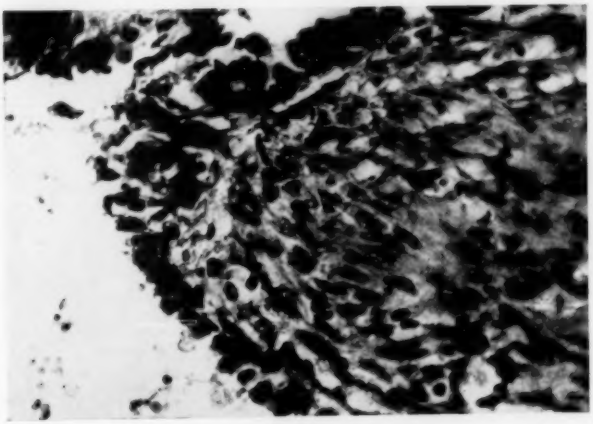

FIG. 3
Case 1. Mülleroma. ×382.

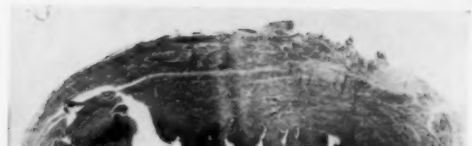

FIG. 4
Case 2. Mülleroma. ×2·66.

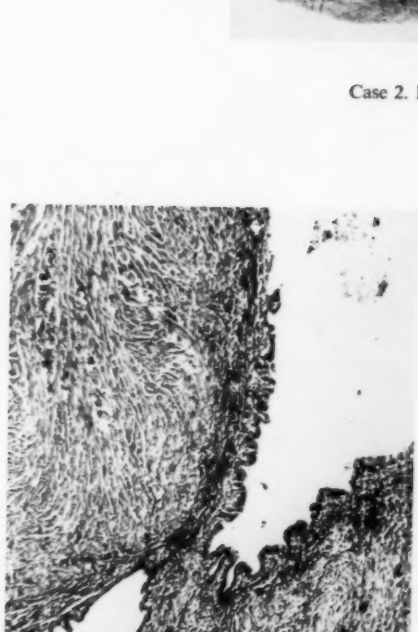

FIG. 5
Case 2. Myometrium, endometrial stroma and epithelium. ×29.

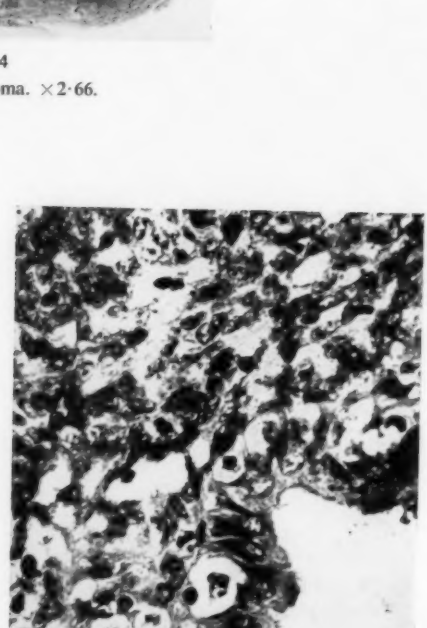

FIG. 6
Case 2. ×353.

was well and there were no associated symptoms. Examination under anaesthesia showed what was thought to be a fibroid about 4 cm. in diameter in the region of the left uterine cornu. It was thought that myomectomy might jeopardize the patency of the left tube and it was decided not to undertake laparotomy, but with her next period her pain was so severe that operation seemed inevitable. A small rounded mass about 1½ inches (4 cm.) in diameter was found lying between the layers of the broad ligament. This was lying within the connective tissue of the broad ligament and had no capsule, no plane of cleavage, and no definite ligamentary supports. It was dissected free from its connective tissue surroundings without difficulty and the abdomen closed. No other lesion was discovered in the pelvis. This operation led to immediate relief of her symptoms and there has never been any more dysmenorrhoea. Since then she has had four pregnancies, two ending in abortion at 8 weeks, but the other two being completed normally, the last early in 1960.

The tumour consisted of a thick-walled muscular organ with a small central cavity about ½ inch in diameter containing dark blood (Fig. 1). Histological examination confirmed the fact that there was a muscular wall with an epithelial lining similar to the endometrium (Fig. 2) and this was confirmed by high power views (Fig. 3).

*Case 2*

G.M.P., aged 34, complained of hypogastric pain and low back pain of about 8-years duration, with exacerbations two days before the beginning of her period and improving when the period ended. This pain began after the birth of her first child and became more severe three years later after the birth of a second child. Conservative treatment with androgens and diathermy was unhelpful. Laparotomy in August, 1954, showed a small tumour between the layers of the right broad ligament which was about 2 cm. in diameter with a muscular wall surrounding an irregular cavity with a yellowish lining (Fig. 4). Microscopy showed the lining to consist of endometrium showing stroma and a covering of tall secretory epithelium (Figs. 5 and 6). After removal of the tumour there was relief of pain for about twelve months but later she developed further lower abdominal pain and hysterectomy was carried out, when well-marked endometriosis was found. This had developed since the previous laparotomy eighteen months earlier. There has been no further pain until July, 1960, when acute pain of three days duration arose as a result of an acute appendicitis. Appendicectomy was carried out with complete relief of this pain.

## Discussion

These two cases of dysmenorrhoea both showed a lesion conforming to the description of Mülleroma by Conill Serra (1950). The first patient was the more typical, being 20 years of age and free from dysmenorrhoea until the late teens when increasingly severe pain brought her to hospital. Ultimately this pain became so severe that she was prepared to accept "any kind of mutilation, if necessary, to end her pain" (Conill Serra, 1950). The second case is less characteristic in that the pain developed six or seven years later than in the other cases described, possibly as a result of the influence on the Mülleroma of the increased hormone levels associated with her pregnancies. It is noteworthy that in each instance pregnancy was followed by worsening of her symptoms. This patient also differs from the others in that only temporary relief of pain was achieved by removal of the Mülleroma, the recurrence of dysmenorrhoea being due to the development of endometriosis of which, however, there was no sign at the original operation. In each instance the tumour was found between the layers of the broad ligament in relation to the uterine cornu, and showed the features of a Mülleroma as described by the Conills, namely a thick muscular coat surrounding a central cavity lined by typical endometrium and containing altered blood. I agree with the opinion of the Spanish authors that this appears to be a distinct lesion, quite unlike endometriosis and adenomyosis and anatomically quite different from the rudimentary horn of a bicornuate uterus in its relation to the tube and to the round and ovarian ligaments. These cases described above appear to be the sixth and seventh, all the others

having been described by Conill and Conill Serra in Barcelona.


## Summary

Two cases of severe dysmenorrhoea obtained complete relief of pain following the removal of a small tumour from the broad ligament.

In each instance, examination of the tumour showed the features of a Mülleroma, a small atretic accessory uterus believed to arise from an accessory Müllerian duct or from abnormal localization of part of the duct itself.


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# INNOCENT DEPRESSION OF THE S-T SEGMENT AND FLATTENING OF THE T-WAVE DURING PREGNANCY

BY

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DURING examination of antenatal patients referred to a cardiac clinic it was noticed that in some the electrocardiogram showed depression of the S-T segment with low voltage T-waves in the absence of evidence of cardiac disease. A frequent reason for requesting an opinion on the heart was that a systolic murmur had been discovered during routine antenatal examination. In such patients the additional finding of an unusual cardiogram might be considered confirmatory evidence of organic heart disease when, in fact, none exists.

The electrocardiogram in pregnancy has been the subject of extensive study, but changes in the precordial S-T segment receive little mention in the literature. Burwell and Metcalfe (1958) do not discuss shift of the S-T segment in their book, neither do de Bettencourt and Fragoso (1952) in their review of the cardiographic changes in 115 cases of normal pregnancy. Amongst the 25 normal pregnant women studied by Zatuchni (1951) S-T segment elevation was a common finding in the precordial leads, particularly in V2 and V3, but S-T depression was reported only once, and then affected V6 alone. Vara and Halminen (1946) found that the S-T segment remained isoelectric in their 60 normal pregnant patients.

Since the electrocardiographic changes to which we draw attention do not appear to have been described previously, and are of such a nature that cardiomyopathy of pregnancy might be suspected, further investigation seemed worthwhile.

## MATERIAL AND METHODS

This report is based on the findings in 100 normal pregnant patients referred by obstetric colleagues at two hospitals. For comparison purposes we also studied the cardiograms of 100 non-pregnant healthy women of child-bearing age.

At the initial visit, after a full history had been obtained, clinical examination was carried out and a 12-lead electrocardiogram and X-ray of the chest were taken. Clinical examination and cardiogram were repeated at each visit, the patients being seen as far as possible once during each trimester of pregnancy, and again within a few months after delivery. No patient was included in the series if there was any doubt as to the complete normality of the cardiac findings, and the few patients who developed toxaemia or other abnormality whilst under observation were also excluded.

TABLE I

*Summary of Cardiographic Findings*

| Case No. | Age | Parity | Rate per Minute | P-R (sec.) | Q-Tc (sec.) | Leads Affected | | Maximum Depression of S-T Segment (mm.) | Minimum Height T-wave (mm.) in L.V. Leads |
|---|---|---|---|---|---|---|---|---|---|
| | | | | | | Limb | Precordial | | |
| 1 .. | 24 | 0 | 100 | 0·16 | 0·41 | I, II, VL | V3,4,5,6 | 1·0 | 0·0 |
| 2 .. | 31 | 1 | 72 | 0·12 | 0·39 | I, II, VL | V5,6 | 1·0 | 1·5 |
| 3 .. | 20 | 0 | 68 | 0·14 | 0·445 | I, II, VL | V2,3,4,5,6 | 0·5 | 0·5 |
| 4 .. | 16 | 0 | 94 | 0·16 | 0·45 | I, II | V3,4,5,6 | 0·75 | <0·5 |
| 5 .. | 33 | 1 | 100 | 0·12 | 0·435 | I, II, VF | V4,5,6 | 0·75 | 1·0 |
| 6 .. | 28 | 1 | 94 | 0·18 | 0·45 | I, VL | V5,6 | 0·5 | 0·75 |
| 7 .. | 34 | 0 | 70 | 0·12 | 0·43 | I, II, VF | V3,4,5,6 | 0·5 | 1·0 |
| 8 .. | 21 | 1 | 107 | 0·12 | 0·45 | I, II | V3,4,5,6 | 0·5 | 1·0 |
| 9 .. | 33 | 0 | 79 | 0·12 | 0·45 | I, II, VL | V3,4,5,6 | 0·5 | 1·25 |
| 10 .. | 31 | 5 | 110 | 0·14 | 0·43 | II, III, VF | V4,5 | 1·0 | 1·75 |
| 11 .. | 33 | 0 | 94 | 0·18 | 0·45 | VF | V4,5,6 | 0·5 | 1·0 |
| 12 .. | 31 | 0 | 84 | 0·14 | 0·40 | II, VF | V5,6 | 0·75 | <0·25 |
| 13 .. | 31 | 0 | 72 | 0·10 | 0·45 | II, III, VF | V5,6 | 0·5 | 2·0 |
| 14 .. | 19 | 0 | 88 | 0·14 | 0·41 | II, VF | V3,4,5,6 | 1·0 | <0·25 |

## RESULTS

Of the 100 normal pregnant women studied, 14 showed S-T changes affecting both limb and chest leads, and it is with these patients that this report is concerned. However, it is of interest that in another 28 cases there were changes of similar character but limited to one or more of the limb leads.

The type of change noted was sagging of the S-T segment, which was depressed to a depth of 0·5 to 1·0 mm., the T-wave in the same lead usually being of low voltage (Table I). There was no depression of the P-R segment, such as may occur in tachycardia. The leads affected were mainly those from the left side of the precordium, V3 to V6 in most instances, the limb leads being involved according to cardiac position. As the cardiac position was predominantly electrically horizontal the limb lead changes in nine patients were confined to lead VL and hence standard leads I and II (Fig. 1) and in the remaining five patients the heart was vertical and thus the limb leads affected were VF and hence II and III (Fig. 2). In no case was there abnormal T-wave inversion, although the T-wave was isoelectric in one of the records (Case 1, leads V4–6), and almost isoelectric, being less than 0·5 mm. tall in three others (Case 4, lead V6; Case 12, lead V4; Case 14, lead V6). The P-R and corrected Q-T intervals (Q-Tc) are commented upon later and are given in Table I.

In affected patients these changes were usually seen in the earliest record available, and showed no material variation during the course of the pregnancy. Twelve of the fourteen patients were re-examined at periods varying from two weeks to seven months after delivery. At this stage all showed a decrease in the severity and extent of the changes, and in four cases, all seen within a month of delivery, the records were completely normal. Those showing persistent changes were further recalled two years after the pregnancy by which time one more record had become normal, three showed further regression of the changes and one was unaltered. Two patients could not be traced and the remaining one was three months pregnant at the time of her visit and had cardiographic changes even more striking than those present during her first pregnancy.

Amongst the control series of 100 non-pregnant females of child-bearing age and free from cardiac disease there were six whose

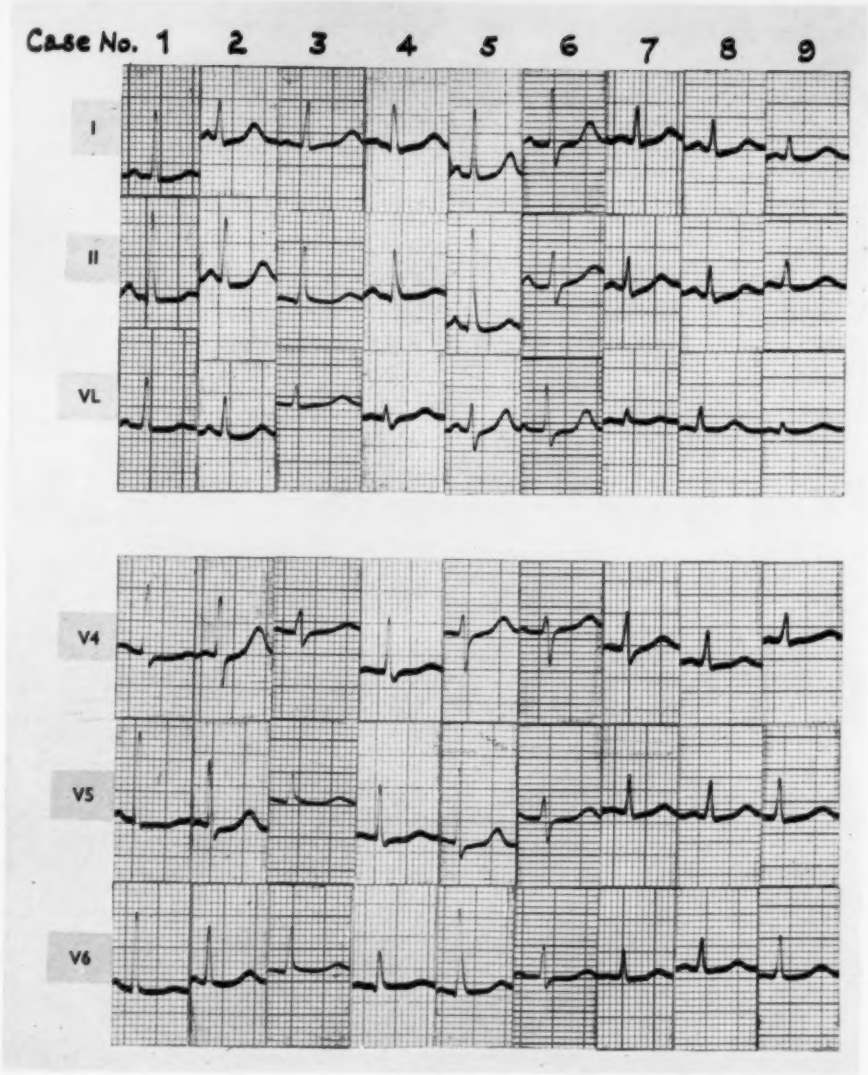
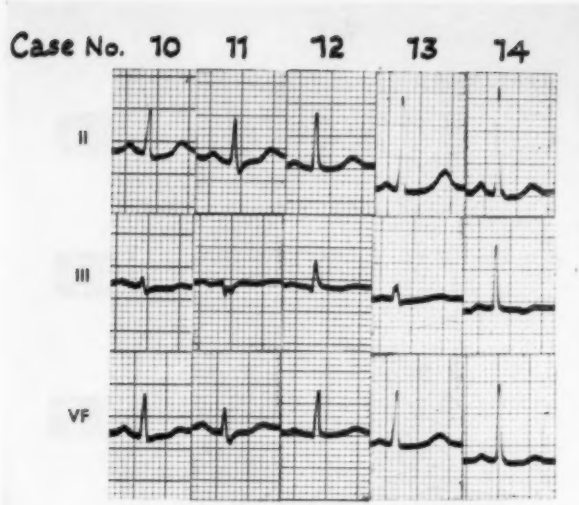



FIG. 1

Selected limb leads (I, II and VL) and chest leads (V4, V5 and V6) of nine patients with electrically horizontal hearts. For description of changes see text and Table I.



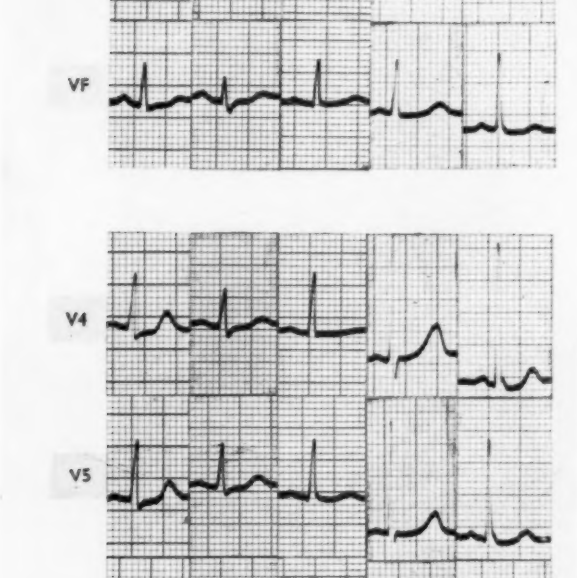




FIG. 2

Selected limb leads (II, III and VF) and chest leads (V4, V5 and V6) of five patients with electrically vertical hearts. For description of changes see text and Table I.

cardiograms showed S-T segment and T-wave appearances of the type described in the pregnancy group.

## Discussion

During recent years it has been increasingly realized that the cardiogram may show wide variation from the accepted normal in the absence of demonstrable heart disease. Littman (1948) and Goldman (1960) both described examples of persistent abnormality of the precordial T-waves, in some instances associated with elevation of the S-T segment, in persons showing no other evidence of cardiac disease, and concluded that such cardiographic changes should not be the sole criterion for a diagnosis of organic heart disease.

Studies based on large numbers of normal subjects seem to indicate that depression of the S-T segment in the precordial leads is not a frequent occurrence, no significant changes being recorded amongst the air force personnel examined by Manning (1954) and Packard *et al.* (1954), although Leatham (1950) found S-T depression of 1 mm. in lead V6 in three of his hundred cases; in the same groups of patients a T-wave voltage of less than 1 mm. in the apical leads was exceptional. The subjects studied by Manning (1954) and Packard *et al.* (1954) were all males, and Leatham's (1950) series included very few women, so that the results are not directly applicable to our pregnancy cases. The effect of sex on the electrocardiogram has been given surprisingly little attention in the literature and we have been able to find only one paper, by Simonson *et al.* (1960), specifically devoted to this aspect of electrocardiography. They make no mention of S-T shift, and unfortunately the age range of their patients was from 40 to 59 years.

With a view to providing a better basis for comparison we studied the cardiograms of 100 non-pregnant women of child-bearing age who showed no evidence of cardiac disease, and of these six had T-wave and S-T segment changes similar to those found in the pregnancy series, thus suggesting that this cardiographic variant may be commoner in women than men. However, in view of the higher incidence during pregnancy, it is pertinent to consider whether any of the factors known to cause S-T segment depression, with or without reduction in voltage of the T-wave, are likely to be in operation at this time.

### *Drug Therapy*

The effect of digitalis in causing sagging of the S-T segment can be excluded in this series, and no other drugs likely to influence the cardiogram were being given.

### *Racial Factors*

The series included only one coloured patient and her electrocardiogram did not show any abnormality. In any case the changes described in the so-called "juvenile pattern" in adult negroes are unlike those under discussion here in that they affect mainly the right-sided precordial leads and consist of elevation of the S-T segment with inversion of the T-wave, as described by Wasserburger (1955) and Greene and Kelly (1959).

### *Hypokalaemia*

Hypokalaemia of sufficient degree to give rise to depression of the S-T segment and changes in the T-wave has been reported as a result of persistent vomiting during pregnancy (Lans *et al.*, 1953). However, in our series only one patient had serious vomiting, and here there were no changes either in the cardiogram or in the serum electrolytes. A history of vomiting in early pregnancy was given by 21 per cent of the group showing S-T depression as compared with 8 per cent of the whole series, but as the vomiting had usually ceased some weeks before the first cardiogram was recorded it seems highly unlikely that electrolyte disturbance could persist long enough to be responsible for the cardiographic changes.

### *Tachycardia*

Tachycardia normally leads to depression of both the P-R and S-T segments, and records showing such an appearance were excluded from analysis. Tachycardia of 100 per minute or more was present in at least one record from eight of the fourteen patients in whose cardiograms S-T

changes were present, the incidence in the group as a whole being lower (29 of 100), but the changes did not appear to be directly related to tachycardia, and when the S-T segment depression was present it remained constant despite variation in heart rate.

*Posture*

Mayerson and Davis (1942) found that the maintenance of an erect posture for a period sufficient to produce impairment of venous return can cause decreased amplitude of the T-wave, but the accompanying S-T depression usually affects the junctional region only. It could be postulated that impairment of venous return might be produced by the gravid uterus, but in that case one would not expect any cardiographic changes so produced to appear early in pregnancy, and they might be expected to increase as the pregnancy advances. The changes which we describe affected the whole of the S-T segment, and showed no significant variation with the stage of pregnancy.

*The Suspended Heart Syndrome*

This variation in intra-thoracic anatomy first described by Evans and Lloyd-Thomas (1957) may be accompanied by cardiographic findings very similar to those occurring in our patients. However, it differs in distribution, the postero-apical leads being those mainly affected, in contrast to our cases in which the changes were predominantly antero-apical. Although the exact mechanism by which the changes are produced remains uncertain both Evans and Lloyd-Thomas (1957) and Bradlow and Zion (1958) consider alteration in the relationship of the heart to its environment to be the basic factor, and it is conceivable that this could also be of significance in pregnancy. Thus the heart in the suspended heart syndrome is vertical and rotated around its longitudinal axis in a clockwise direction as viewed from below, while the heart in pregnancy tends to lie transversely, even during the early months, without significant longitudinal rotation (Zatuchni, 1951).

*Effect of Food*

It has been shown that a high carbohydrate meal may be followed by transient flattening or even inversion of the apical T-wave with depression of the first part of the S-T segment, and that the changes are particularly striking after oral glucose (Rochlin and Edwards, 1954; Rosen and Gardberg, 1957). Similar cardiographic findings have been demonstrated by Pulvertaft (1954) in the so-called "dumping" syndrome, where they appear to be related to the rate of absorption of sugar. The majority of the patients in our series were examined two or three hours after food but no variation was noted in those where the record was repeated at some other time of day.

*Anxiety*

The effect of psychological stress on the cardiogram has received much attention (Wendkos and Logue, 1946; Plice and Pfister, 1950; Magendantz and Shortsleeve, 1951), and the appearances described bear a close resemblance to those seen in the pregnant patients reported here. Most authorities attribute the changes to autonomic imbalance but the exact mechanism remains in dispute (Wilde, 1958). Levine *et al.* (1930) showed that adrenaline given subcutaneously produced lowering of the T-wave voltage in the standard lead cardiograms of five out of ten healthy young adults, whilst a substantial dose of the drug given intravenously could produce actual T-wave inversion. Mitchell and Shapiro (1954) described the findings in a woman with anxiety state whose cardiogram recorded at a time of emotional stress showed changes closely resembling those seen in our pregnant patients, and in whom intravenous adrenaline could also reproduce these effects. Two other patients who were regarded as emotionally stable, and another with cardiac neurosis did not show this response to adrenaline, and the authors postulate that in some individuals the myocardium is particularly sensitive to the effect of adrenaline, and that in them these cardiographic effects can be evoked by anxiety-producing stimuli.

It seems likely that anxiety was a significant factor in our cases since, when evidence of nervousness was particularly noted at each visit, such signs proved to have been present in 36 per cent of those patients showing abnormalities on the cardiogram compared with only

13 per cent of those whose cardiograms were normal. Additional evidence is found in the striking disparity in the incidence of cardiographic change between the two hospitals from which cases were drawn. Although equal numbers of patients were contributed from each hospital only four of the fourteen examples showing cardiographic abnormality came from the clinic where the nature of the investigation was explained to the patients and their co-operation sought, the majority being found in the second group who were referred to a cardiac clinic together with patients with cardiac disease and who might, therefore, be expected to have experienced some anxiety regarding their heart condition.

Some further evidence that the changes which we have described may be at least associated with a sympathicotonic state is found by measurement of the P-R and Q-T intervals. The upper limit of the P-R interval is usually accepted as at least 0·02 second, if not 0·22 second, and it is known to be shorter in states where excessive adrenaline is being produced. In none of our series did it reach 0·2 second, the range being 0·01 to 0·18 second, and the average 0·13 second (see Table I).

The Q-T interval becomes shorter as the cardiac rate increases, but when it is corrected for rate (Q-Tc) by, for example, the formula of Taran and Szilagyi (1947) it is found to increase in sympathicotonic states. The upper limit for the Q-Tc duration in women is 0·42 second. In only four of our patients did it fall below this figure and in the remaining ten it exceeded it.

Wasserburger and Lorenz (1956) reported the abolition of depression of the S-T segment and improvement in the flattened T-waves which occurs in emotionally unstable subjects by the use of the vagal-blocking agent propantheline bromide, preferably given intravenously. It therefore seemed worth trying this drug in our patients. The intravenous route had to be abandoned as the induced tachycardia proved so distressing that the discomfort was considered unjustifiable, and in the remainder of the patients the cardiogram was recorded after three days' oral administration of propantheline in a dose of 15 mg. four times a day. The results were, however, unimpressive and the investigation was discontinued after six cases had been studied. Of these the record reverted to normal in only one patient, four showed no material change, and in the remaining one there was actually deterioration.

*Hyperventilation*

Severe hyperventilation has been shown to produce flattening of the T-wave and in some cases S-T depression also (Thompson, 1943), particularly in the presence of other factors causing this type of cardiographic change such as anxiety (Wasserburger and Lorenz, 1956). The findings in the cardiogram do not correlate at all closely with the shift in blood pH, and Scherf and Schlachman (1947) suggested that the effects were postural due to lowering of the diaphragm. Studies of respiratory physiology in pregnancy (Burwell and Metcalfe, 1958) indicate that a degree of hyperventilation is normal, and this would, of course, be more severe in the nervous patient.

## Conclusions

In view of the lack of corroborative evidence of cardiac disease, the subsequent benign course of the pregnancy and the fact that the cardiographic changes diminished or disappeared after pregnancy in all cases, there seems no reason to regard the cardiographic features described as in any way signifying an abnormal state. It is apparent from the multiplicity of conditions in which depression of the S-T segment has been described that this is a non-specific change which can be produced in susceptible persons by a variety of factors. Pregnancy, or circumstances associated with it, appears to be playing an essential part in the examples recorded here as the incidence of this type of change in the cardiogram was more than doubled in the pregnancy series compared with a control group of non-pregnant women. However, it seems unlikely that there can be any direct correlation with the physiological alterations in the circulation, or electrolyte disturbance, occurring during pregnancy in view of the lack of change in the pattern of the cardiogram as pregnancy advances.

The higher incidence of cardiographic involvement amongst patients showing evidence of

nervousness suggests that anxiety may play an important part in producing these changes, probably acting in conjunction with factors peculiar to pregnancy such as alteration in cardiac position. The mechanism by which anxiety produces these effects remains uncertain but the presence of myocardial sensitivity to adrenaline in some individuals would be consistent with the persistence of the cardiographic changes after delivery in some of our patients, and also the occurrence of a similar cardiographic picture in an appreciable number of the non-pregnant women used as controls, a high proportion of whom had attended with some form of cardiac neurosis.

## Summary

Attention is drawn to the frequent occurrence during normal pregnancy, 14 per cent of 100 patients, of cardiographic changes which might give rise to a suspicion of cardiomyopathy. The type of change noted was sagging of the S-T segment, which may be depressed to a maximum depth of 1·0 mm., the T-wave in the same lead usually being isoelectric or of low voltage but not frankly inverted. The left-sided precordial leads were those mainly affected, the limb leads being involved according to cardiac position. Similar changes were found in the cardiograms of 6 per cent of 100 healthy non-pregnant women of child-bearing age.

The possible causation of these changes is discussed and it is concluded that anxiety is probably the main factor in their production, acting in conjunction with factors peculiar to pregnancy such as alteration in cardiac position.

The main thesis of this paper is not so much to offer a firm explanation of the electrocardiographic changes which have been described, but rather to draw attention to them and to emphasize both their frequency and innocent nature.

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# CERVICAL CYTOLOGY AND INTRA-EPITHELIAL CANCER OF THE CERVIX IN PREGNANCY

BY

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## INTRODUCTION

THE main purposes of this communication are to consider firstly the place of routine cervical cytology in obstetric patients, and secondly the diagnosis of intra-epithelial cancer of the cervix in association with pregnancy. The whole question of intra-epithelial (*in situ*, pre-invasive) cancer is sufficiently contentious, however, to warrant a brief survey of current opinion on the subject.

## CYTOLOGY

Cytology is now generally accepted as a most useful aid in the detection of cancer—and especially of early cancer—in many parts of the body. Much of the credit for this acceptance is due to Papanicolaou and Traut whose monograph, published in 1943, was responsible for the beginning of world-wide recognition of gynaecological cytology. It is worth recalling that Papanicolaou had already reported in 1928 that cancer cells could be detected in vaginal smears. Moreover, as long ago as 1878, Lionel Beale, Professor of Medicine at King's College Hospital, London, had written: "In cases of cancer of the uterus we should expect to meet with cancer cells in the discharges." He had proceeded to describe a method for obtaining these cells which is almost identical to one of the "modern" smear techniques.

## INTRA-EPITHELIAL CANCER

*Natural History.* A direct result of the widespread adoption of "routine" cervical cytology has been the emergence of intra-epithelial cancer as a definite and not uncommon entity, from being an interesting and relatively rare histological diagnosis. This in turn has resulted in a number of problems of which the most difficult relate, firstly, to the exact nature of the condition and, secondly, to its ultimate course. There is now fairly general belief that the lesion is in fact pre-invasive, and if not treated will, in at least a proportion of cases, progress to invasive cancer. Unfortunately proof of this belief depends on a satisfactory study of the undisturbed lesion and such a study is not at present possible. The diagnosis of intra-epithelial cancer of the cervix cannot be made on clinical or cytological criteria, but is dependent on histological examination of the cervix. Moreover the investigation of a positive smear from a clinically unsuspicious cervix—the "surprise positive"—demands a full cone biopsy. Anything less extensive is not only inadequate but negligent because there is ample proof that up to 10 per cent of such cases will show invasive cancer (Table I), which may not be seen in the more limited wedge or punch biopsies. Thus Greene and Peckham (1958) found that in 138 cases where a diagnosis of intra-epithelial cancer had been made on the basis of four-quadrant biopsies, the subsequent conization or hysterectomy revealed co-existent and unsuspected invasion in 3·8 per cent. On the other hand, conization will frequently remove all the malignant tissue, thus becoming a therapeutic as well as a diagnostic measure and preventing study of the natural history of the undisturbed lesion. For these reasons the findings of Petersen (1956), although surely of considerable

TABLE I

*Comparison of Surprise Positive Cancer Rates, and Percentage of Cases of Invasive Cancer*

| Author | Type of Patient | No. of Patients | Surprise Positive Rate per Thousand Patients | Proportion of Invasive Cases as Percentage of All Surprise Cases |
|---|---|---|---|---|
| Dahlin *et al.* (1955): | | | | |
| (*a*) all patients | Gynaecological | 30,310 | 8·9 | 8·9% |
| (*b*) under 40 years of age | Gynaecological | 12,912 | 8·5 | 3·6% |
| McLaren *et al.* (1956) | Gynaecological | 2,250 | 4·4 | 11·1% |
| Carey and Williams (1958) | Gynaecological | 8,951 | 2·4 | 18·2% |
| Present survey | Obstetric | 3,295 | 3·0 | 10·0% |
| Spujt *et al.* (1960) | Obstetric | 3,352 | 2·1 | 0% |

significance, cannot be accepted as necessarily indicative of the true course of intra-epithelial cancer. In his series of 127 cases, untreated except for the original biopsy, 33 per cent had progressed to invasion at the end of 9 years. The initial investigation of some of these cases was by limited biopsy only (Petersen, 1955) and may not have excluded invasion already present. Others may have been completely cured by cone or even wedge biopsy.

Some knowledge of the average duration of the intra-epithelial phase before its progression to invasive cancer has been obtained by comparing the respective age incidences of the two conditions. Hertig and Younge (1952) found the average ages to be 38·7 and 48 years respectively. Mussey and Soule (1959) surveyed 842 intra-epithelial cases treated at the Mayo Clinic between 1932 and 1957 and found a mean age of 43·4 years against a mean of 49 years for invasive cases. Dunn (1953) points out that it is logical to assume that the average intra-epithelial cancer should be at the mid-point of its slow evolution when discovered. It is reasonable then to suggest that the actual duration of this phase prior to invasion may average upwards of 15 years.

Information on a much more important point is even more scanty—namely, what proportion, if any, of cases of invasive cancer have a short or even transitory intra-epithelial phase? On this will depend the urgency which is to be accorded to a diagnosed case, and also the period of relative security conferred by a negative cytology report. The interim results reported by Erickson *et al.* (1956) suggest that this proportion may be relatively high. Repeat cytological examinations of 32,000 women with negative reports 1 to 2 years previously, led to a diagnosis of 5 surprise cases of invasive cancer, a rate of 0·15 per 1,000 which is approximately 25 to 30 per cent the expected rate in a previously unscreened population group (Table I). The inference is that perhaps a quarter to a third of all invasive cases progress through the intra-epithelial phase in less than 2 years. (A further inference is that many intra-epithelial lesions must remain so for far longer than 15 years.)

*Treatment.* The methods of treatment for intra-epithelial carcinoma of the cervix have varied widely. Mussey and Soule (1959) record no fewer than 13 different modes in 842 cases, ranging from simple electro-cautery through Wertheim hysterectomy to high dosage irradiation. Recent years have seen a world-wide trend towards less radical measures. Irradiation has been almost abandoned. Hysterectomy is the most popular procedure but this too is losing favour in selected cases in the face of increasing information regarding the efficacy of radical conization. Thus Krieger and McCormack (1958) reported 61 cases followed for 6 months to 7 years after conization with no cases developing invasive cancer.

*In Association with Pregnancy.* The extension of the smear programme to obstetric patients has resulted in further problems. Not the least of these has been a general acceptance of the

belief that pregnancy, *per se*, may cause changes in the cervical epithelium indistinguishable from intra-epithelial cancer, and that such changes may regress spontaneously and completely with the termination of the pregnancy (Epperson *et al.*, 1951; Nesbitt and Hellman, 1952). This concept has been challenged strongly by a number of writers and the consensus of opinion is now moving towards a belief that intra-epithelial cancer in and out of pregnancy is one and the same lesion. Marsh and Fitzgerald (1956) reported 18 cases in all of which the condition persisted after pregnancy. Greene and Peckham (1958) have a series of 37 cases followed for varying periods with a persistence of the lesion in 29. They explain the disappearance of the disease in the other 8 as being due in some cases to spontaneous regression, and in others to complete removal of the lesion in the original biopsy. A similar disappearance is equally common in the non-pregnant, the rate of disappearance being, as expected, proportional to the extent of the original biopsy. Krieger and McCormack (1958) reported 28 cases diagnosed by conization and treated 6 weeks later by hysterectomy with residual disease evident in 4 only.

Another major problem in pregnancy arises from the vascularity of the pregnant cervix. It is now standard practice in most centres to employ radical conization with scalpel or trachelotome as the routine method of investigation of surprise positive smears. Even in the non-pregnant state a 20 per cent morbidity rate, chiefly pyrexia and/or haemorrhage, has been reported following such biopsies (Boyd, 1958). In pregnancy the risk of haemorrhage can be expected to be disproportionately high for which reason conization has been avoided and less extensive wedge biopsies taken. As previously noted this practice may give false results. Ferguson and Cavanagh (1959) however state that the hazards of biopsy in pregnancy are reduced by infiltration of the cervix with adrenaline saline solution. (Scott *et al.*, 1960, recommend a similar technique in the non-pregnant patient.) They report 13 cone biopsies, including 4 in the last trimester, without significant haemorrhage. Seven out of 10 of the pregnancies, however, terminated in premature deliveries (birth-weight less than 2,500 g.) with two consequent foetal deaths. This must be considered to be a possible complication of the operation.

## Material

The present survey covers patients attending the obstetric clinics (antenatal and postnatal) at the National Women's Hospital, Auckland, between 1st July, 1957 and 30th June, 1959. Hospital policy is that cervical smears be prepared at the "booking" clinic from all obstetric patients over the age of 29 years and from any younger woman at the discretion of the examining doctor. In practice this has meant that some attendants have taken smears from all patients, irrespective of age or parity, while others have restricted them to older women only. Any patient found to have a cervical erosion at examination 6 weeks after delivery has a further smear taken. (She returns for electro-cautery treatment after a further six weeks if the lesion persists.)

In the period under review 4,829 new patients have been examined, and 3,515 smears have been prepared from 3,295 women. There is therefore some selection of material. There has, however, been at least comparable selection in any group of women attending a gynaecological clinic, and comparison of incidences of surprise positive results is valid.

As this paper is in part an attempt to evaluate a programme of routine cytology in obstetric patients, 2 cases of intra-epithelial cancer of the cervix, which were first referred to the antenatal clinic because of abnormal cytology, are excluded, as is a case where a surprise positive smear taken at the booking clinic led to the same diagnosis in a woman found to be not pregnant.

Cases where the appearance of the cervix aroused sufficient suspicion of malignancy to warrant biopsy are not classed as "surprise positive" and are not included.

## Methods

Ayre's technique has been employed, whereby a wooden spatula, split lengthwise, is placed in the external os and rotated to scrape the squamo-

columnar junction. The initial screening of the smear is by laboratory technicians. Doubtful and suspicious smears are referred to the pathologist who issues the final report. The term "positive cytology" as used here does not include those smears showing atypical cells only.

With the exception of one case investigation has been by cone biopsy of the cervix. This does not mean a gentle excision of the squamo-columnar junction (the "ring" biopsy), but is a true conization, taking a wide circle around the external os and extending deeply into the cervical canal. Haemostasis is usually easy to obtain with one or two lateral sutures. No attempt is made to cover the cavity with epithelium, and perhaps the most remarkable feature of its subsequent course is the rapidity with which it heals.

## Results

Surprise positive cytology reports were obtained from 10 cases, an incidence of 3·04 per thousand. Table I compares this incidence with other recent series.

Subsequent investigations led to the diagnosis of invasive cancer of the cervix in 1 case and of intra-epithelial cancer in 9 cases. The detailed data are given in Table II.

In 8 cases the initial abnormal smear was taken at the first antenatal examination. In 2 cases with normal cytology reports from the booking clinic, surprise positive smears were obtained at postnatal examination.

The appearance of the cervix was macroscopically normal in 5 cases. The other 5 showed varying degrees of erosion and infection.

The final diagnosis in all 9 cases of intra-epithelial cancer was reached by cone biopsy after delivery, the interval varying from two weeks to ten months, with 6 being taken three months—or more—post-partum. One had had a limited ring biopsy taken during pregnancy and another had had four-quadrant biopsies taken immediately after delivery. In the tenth case, invasive cancer was diagnosed rather fortuitously in a single wedge biopsy taken during pregnancy.

One patient was 23 years of age, and the others were between 30 and 36 years. Two were pregnant for the first time, with the parity of the others ranging from two to nine.

No false positive results were obtained but the false negative incidence cannot be determined. It must be considered that the initial reports in Cases 4 and 6 were possibly in this category. The discrepancy between the number of patients and the number of smears is accounted for by those cases where the initial smear showed atypical cells or contained insufficient material to allow an adequate opinion to be given.

## Discussion

If pregnancy, *per se*, produces changes in the cervical epithelium indistinguishable from intra-epithelial cancer, the taking of cervical smears during pregnancy should give a high surprise incidence of positive results. Comparison with other series in Table I shows that this is not the case. If the condition regresses spontaneously after delivery, delayed biopsy should result in false positive reports in pregnancy. This has not eventuated and 6 of 7 cases subjected to cone biopsy three months or more post-partum still showed malignant tissue. The seventh case had previously had a full cone taken two weeks after delivery. Such results support the contentions that if intra-epithelial cancer of the cervix is found in association with pregnancy, the pregnancy is coincidental and not causal, and that the lesion will persist after termination of the pregnancy.

The partial restriction to patients over the age of 30 years is reflected in the age incidence of the cases diagnosed. Of the 20 cases presented by Marsh and Fitzgerald (1956), 11 were under 30 years of age. Moreover, Dahlin *et al.* (1955) report an incidence of 5·6 cases per thousand among 4,240 women aged 20 to 29 years, compared with 9·8 per 1,000 in 8,480 women aged 30 to 39 years. This suggests that the restriction imposed in this series is unwise, and that all obstetric patients should have cervical smears taken. The antenatal clinic presents an opportunity to screen a wide section of the community which might not otherwise be accessible.

TABLE II

*Detailed Data of Surprise Positive Cases of Cancer of the Cervix*

| Case No. | Age | Parity | Duration of Pregnancy | Appearance of Cervix | Cytology Report | Investigation | Time of Investigation | Diagnosis | Further Treatment | Remarks |
|---|---|---|---|---|---|---|---|---|---|---|
| 1 | 30 | 0 | 14 weeks | Erosion | Positive | 1. Ring biopsy<br>2. Cone biopsy | 1. 17 weeks<br>2. 8 weeks p.p. | 1. Carcinoma *in situ*<br>2. Carcinoma *in situ* | — | — |
| 2 | 36 | 4 | 1. 20 weeks<br>2. 38 weeks | Normal<br>Normal | Atypical<br>Positive | Cone biopsy | 7 weeks p.p. | Carcinoma *in situ* | Hysterectomy 6 weeks later | Residual Carcinoma *in situ* |
| 3 | 31 | 9 | 1. 22 weeks<br>2. 36 weeks | Normal<br>Normal | Atypical<br>Positive | Cone biopsy | 5 months p.p. | Carcinoma *in situ* | Hysterectomy 6 weeks later | No residual cancer |
| 4 | 35 | 3 | 1. 12 weeks<br>2. 6 weeks p.p. | Erosion<br>Erosion | Normal<br>Positive | Cone biopsy | 7 months p.p. | Carcinoma *in situ* | — | — |
| 5 | 33 | 6 | 38 weeks | Normal | Positive | Cone biopsy<br>Cone biopsy | 2 weeks p.p.<br>3 months p.p. | Carcinoma *in situ*<br>No carcinoma | — | — |
| 6 | 23 | 0 | 1. 12 weeks<br>2. 6 weeks p.p. | Normal<br>Erosion | Normal<br>Positive | Cone biopsy | 10 months p.p. | Carcinoma *in situ* | — | — |
| 7 | 30 | 8 | 1. 16 weeks<br>2. 24 weeks | Erosion<br>Erosion | Atypical<br>Positive | Cone biopsy | 3 months p.p. | Carcinoma *in situ* | For Hysterectomy | — |
| 8 | 36 | 2 | 1. 24 weeks<br>2. 8 weeks p.p. | Normal<br>Erosion | Atypical<br>Positive | Cone biopsy | 3 months p.p. | Carcinoma *in situ* | Hysterectomy 5 months later | No residual cancer |
| 9 | 33 | 2 | 1. 20 weeks<br>2. 24 weeks | Normal<br>Normal | Atypical<br>Positive | 1. 4-Quadrant biopsies<br>2. Cone biopsy | 1. Delivery<br>2. 3 months p.p. | Carcinoma *in situ*<br>Carcinoma *in situ* | — | — |
| 10 | 33 | 3 | 22 weeks | Normal | Positive | Wedge biopsy | 23 weeks | Invasive cancer | Radium X-ray | |

N.B.—p.p. = Post-partum.

Analysis of the 138 cases of invasive cancer of the cervix admitted to the National Women's Hospital during the period under survey gives some indication of the immediate benefits which such a programme might confer. Twenty-nine had had a term pregnancy within the 10 years prior to the diagnosis of cancer. Of 15 women under the age of 40 years, 10 had been pregnant within the previous five years and 8 within three years. (These figures exclude the current pregnancy in 6 cases presenting with invasive cancer during pregnancy.) Remembering that the average duration of the pre-invasive phase is probably 15 years or more, how many of these 29 women might have been diagnosed in this phase? Those who still suggest that one is casting too wide a net for too small a catch should bear in mind that the overall 5-year survival rate from invasive cervical cancer remains in the region of 40 per cent. Moreover to quote Way (1959): "To me the future control of cancer of the cervix lies in very much earlier diagnosis, however it be treated, because we have exhausted the possibilities of surgery and just about those of radiotherapy too."

The method and timing of further investigations when positive cytology is reported during pregnancy remains a difficult problem. The dangers to be balanced are, on the one hand, that of cone excision from the pregnant cervix, and on the other the possibility of the lesion being an invasive cancer.

The incidence of invasion as a percentage of all surprise cases in several series is shown in Table I. Dahlin *et al.* (1955) have further analyzed their cases to show the proportion of invasive to non-invasive cancers among surprise cases in each age group (Table III).

It would appear from these figures that the chance of any given surprise case being invasive is not likely to be higher than 10 per cent and in younger women is probably considerably lower.

As previously stated, Ferguson and Cavanagh (1959) discount any immediate danger from cone biopsy during pregnancy, although their experience reveals a possible hazard to the foetus. Experience in this hospital is contrary to their opinion and projected conization during pregnancy, especially during the latter months, has been avoided because of the risk of haemorrhage. It may be that this approach is too conservative.

TABLE III

*Age Distribution of Patients Having Pre-clinical Carcinoma of Cervix*

| Age (years) | Intra-epithelial Carcinoma | Invasive Carcinoma |
|---|---|---|
| 10–19 .. .. .. | 1 | 0 |
| 20–29 .. .. .. | 24 | 0 |
| 30–39 .. .. .. | 83 | 4 |
| 40–49 .. .. .. | 78 | 9 |
| 50–59 .. .. .. | 41 | 6 |
| 60–69 .. .. .. | 15 | 4 |
| 70–79 .. .. .. | 1 | 1 |
| Total .. .. .. | 243 | 24 |
| Average age (years) .. | 42·1 | 49·7 |

On the basis of present knowledge, and with due regard for the various hazards involved, it is suggested that, when a surprise positive cytology report is obtained during pregnancy, a reasonable approach to the problem is as follows:

(1) Younger women (say under 35 years of age): Biopsy delayed until after delivery, irrespective of the present period of gestation.

(2) Older women:
   (*a*) Immediate cone biopsy if the period of gestation is less than 20 weeks.
   (*b*) Biopsy after delivery if the period is more than 20 weeks.

(3) Early induction of labour to be performed when conditions are suitable and the danger of prematurity is passed.

(4) Cone biopsy to be performed two to three weeks after delivery.

Admittedly such positive demarcations according to age and duration of pregnancy are purely arbitrary, but the extent of our present knowledge makes this unavoidable. Admittedly, too, such a scheme will result in a delay in the diagnosis of early invasive cancer in a small proportion of cases, but, because of the limitations imposed by the pregnancy, this too would seem unavoidable if one is to escape the danger of unnecessary biopsy in the much larger group of intra-epithelial cases.

## Summary

Cervical smears have been taken from 3,295 obstetric cases. Surprise positive reports have resulted in the diagnosis of 1 case of invasive cancer and 9 cases of intra-epithelial cancer.

Support is given to the contentions that pregnancy does not cause changes in the cervix simulating intra-epithelial cancer, and that this condition is one and the same lesion, in and out of pregnancy.

The taking of cervical smears from all obstetric patients is advocated.

A scheme for the investigation of surprise positive cytology during pregnancy is presented.



## Acknowledgments

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Table III is reproduced by courtesy of the Editor of *Surgery, Gynecology and Obstetrics.*


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# VAGINAL CYTOLOGY IN PREGNANCY

BY

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THE earliest description of the changes which take place in the vaginal epithelium during pregnancy was made in 1913 by Favarger. In 1925 Papanicolaou described the characteristic navicular cells of pregnancy in the vaginal smear and since then several studies of the exfoliative cytology of pregnancy have been made (Pundel and Van Meensel, 1951; Pierce, 1957; Spira and MacRae, 1960). Despite suggestions from these writers, vaginal cytology has not been widely used as an indicator of hormone balance in pregnancy. The present investigation is an attempt to assess the value of vaginal cytology to the obstetrician.

## MATERIAL AND METHODS

Our knowledge of vaginal cytology was based on a study of more than 1,000 smears taken from 300 patients at different stages of pregnancy, the results being correlated with the patient's clinical condition.

The present investigation consists of 116 abnormal pregnancies of patients who attended the Professorial Unit at Queen Charlotte's Hospital during 1959 and 1960.

Smears of the vaginal secretion aspirated from the posterior fornix were fixed in a mixture of 50 per cent ether and alcohol and stained by the Shorr and haematoxylin method (Osmond-Clarke and Murray, 1958).

## CYTOLOGY

The assessment of the vaginal smear was made from the amount of cell desquamation, the size of the cells, the pattern of the cells and the cornification index. In our opinion these four factors are of equal importance and a pregnancy pattern should never be classified as good if it fails to reach the necessary standard in any of these four categories.

Using these criteria, three groups of smears can be recognized and these have been graded as poor (1), moderate (2) and good (3). A smear is classified as good if (*i*) there is heavy cell desquamation, (*ii*) the cells are small, (*iii*) the pattern of the cells throughout the smear shows clumps which include navicular and basal cells (some of the latter are described as "oyster cells"), and (*iv*) the cornification index is less than 10 (Figs. 1 and 2).

Since the cornification index (C.I.) is generally accepted as a sensitive indicator of the concentration of oestrogen it might at first sight seem anomalous that in a good pregnancy smear the C.I. is low rather than high. However, the C.I. is known to be reduced by anti-oestrogens such as progesterone and androgen and, since progesterone is known to be present in large amounts in normal pregnancy, this could explain the low C.I. Even so, a good pregnancy smear is not identical with a good luteal smear and it

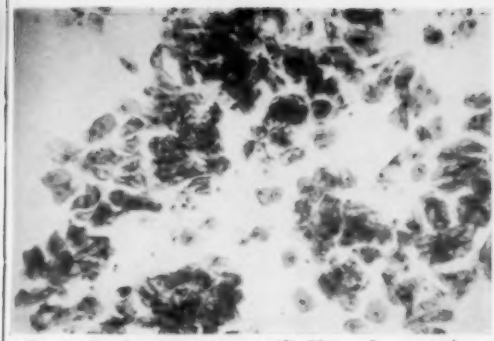


FIG. 1: Good pregnancy smear (3). Heavy desquamation of small cells, generalized pregnancy pattern, low cornification index. × 100.

FIG. 2: Good pregnancy smear (3). "Navicular cells of pregnancy" as described by Papanicolaou. × 400.

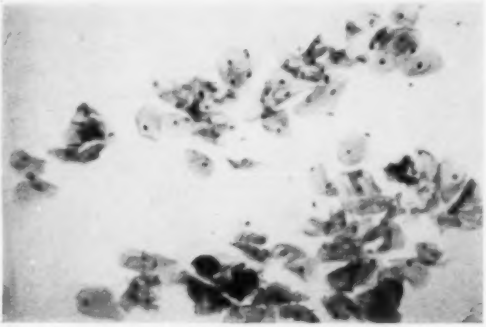


FIG. 3: Threatened abortion at 11 weeks. Aborted one week later. Poor pregnancy smear (1). Desquamation not marked, cells larger and more discrete, no pregnancy pattern, raised cornification index. This smear is similar to that seen in the luteal phase of the menstrual cycle. × 100.

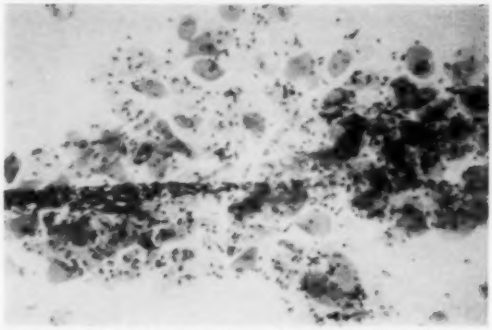


FIG. 4: Threatened abortion at 10 weeks. Aborted two weeks later. Poor pregnancy smear (1). Cervical mucus infiltrated with polymorphs, larger cells with no pregnancy pattern and raised cornification index. This smear is similar to a mild luteal pattern. × 100.

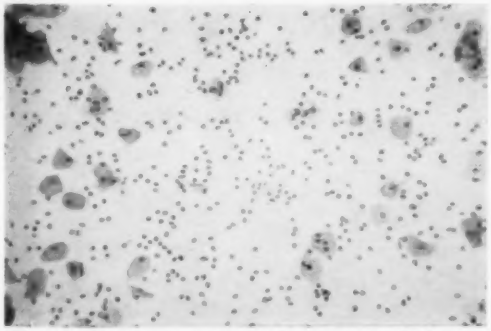


FIG. 5: Foetal death at 39 weeks. Smear taken 24 hours prior to foetal death. Poor pregnancy smear (1). Scanty desquamation of small cells, only slight remains of pregnancy pattern, but low cornification index. × 100.

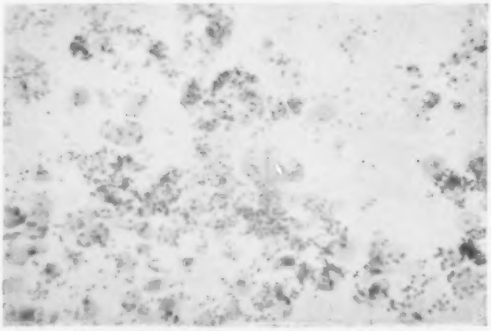


FIG. 6: Foetal death at 36 weeks. Smear taken one week after death. Poor pregnancy smear (1). Reasonable desquamation of slightly larger cells with poor pregnancy pattern but low cornification index. × 100.

may be that another unidentified hormone is acting during pregnancy.

### Threatened Abortion

Threatened abortion is defined as uterine bleeding before the 28th week of pregnancy without evidence of expulsion of the conceptus. The treatment of patients with threatened abortion consisted of rest, sedation and the avoidance of sexual intercourse; no hormone therapy was used. Vaginal smears were taken within two weeks of the uterine bleeding and were repeated at varying intervals until delivery of the foetus.

There were 45 patients with a threatened abortion, 13 of whom had had one or more miscarriages. Thirty-three showed abnormal cytology (Figs. 3 and 4) and of these 16 subsequently aborted (Table I). Of the remaining 12 patients with normal smears only one miscarried; this patient was delivered of stillborn macerated twins at the 26th week of gestation. There was no cytological difference between those patients who first bled before the 12th week of pregnancy and those who first bled after the 12th week (Table II).

Table I

*Relation Between Type of Vaginal Smear and the Outcome of Pregnancy in 45 Patients with Threatened Abortion*

| Type of Smear | Abortion | Pregnancy Proceeded Beyond 28th Week | Percentage Aborted |
|---|---|---|---|
| Normal .. .. (moderate and good) | 1 | 11 | 8·1 |
| Abnormal .. .. (poor) | 16 | 17 | 48·4 |

Table II

*A Comparison of the Vaginal Cytology in Patients Who First Bled Before and After the 12th Week of Pregnancy*

| | Uterine Bleeding Before the 12th Week | Uterine Bleeding After the 12th Week |
|---|---|---|
| Number of patients | 27 | 18 |
| Normal smears .. | 6 (0) | 6 (1) |
| Abnormal smears .. | 21 (10) | 12 (6) |

Number of patients who aborted in brackets.

In 16 out of the 17 patients whose pregnancy proceeded beyond the 28th week the abnormal smears improved, the transition to a normal smear occurring between the 10th and 30th week of pregnancy.

### Normal Pregnancy Following a Past History of Abortion

The cytology was abnormal in 10 of the 19 patients with a normal pregnancy following a previous history of one or more abortions; subsequently, the smears became normal between the 12th and 29th week. All the patients were delivered of live babies although 5 of the 10 with abnormal smears had infants weighing less than 6 pounds.

### Pre-eclamptic Toxaemia and Essential Hypertension

Cytology was carried out in 30 patients with pre-eclamptic toxaemia and 12 with essential hypertension. It was possible to obtain smears throughout the pregnancy of patients with hypertension but only one or two smears were examined in the majority of patients with pre-eclamptic toxaemia as frequently labour was induced soon after the onset of the disease.

Abnormal smears were found in 11 patients and 4 perinatal deaths occurred in this group (Table III). No perinatal loss occurred in the remaining 31 patients with normal smears. In addition, foetal distress and extensive placental infarction were more frequent in those with abnormal smears (Table IV).

Table III

*Vaginal Cytology in Patients with Pre-eclamptic Toxaemia and Essential Hypertension and Its Relation to Perinatal Mortality*

| Type of Smear | Pre-eclamptic Toxaemia (Nos. of Patients) | Essential Hypertension (Nos. of Patients) | Perinatal Deaths |
|---|---|---|---|
| Normal .. | 21 | 10 | 0 |
| Abnormal .. | 9 | 2 | 4 |

TABLE IV

*A Summary of the History of the Pre-eclamptic and Hypertensive Patients with Abnormal Smears*

| Clinical Condition | Cytology | Labour and Delivery | Placenta | Foetus |
|---|---|---|---|---|
| Hypertension (proteinuria 37 weeks) | Abnormal at 36 weeks | Induced 38 weeks Foetal distress | Generalized villous necrosis, infarcts | Death 1 hour after delivery (intra-partum anoxia) |
| Hypertension | Abnormal at 37 weeks | Induced 39 weeks Foetal distress | More than one half infarcted | Alive (asphyxia pallida) |
| P.E.T. 25 weeks | Abnormal at 29 weeks | Normal 31 weeks | Generalized villous necrosis | Death *in utero* 28 weeks |
| P.E.T. 25 weeks | Abnormal at 29 weeks | Premature 30 weeks | Half placenta infarcted | Severe cerebral haemorrhage |
| P.E.T. 28 weeks | Abnormal at 31 weeks | Induced 32 weeks | Generalized villous necrosis | Died after delivery (hyaline membrane) |
| P.E.T. 30 weeks | Abnormal at 33 weeks | Caesarean section 35 weeks | Normal | Alive |
| P.E.T. 36 weeks | Abnormal at 39 weeks | Normal 39¼ weeks | Normal | Death *in utero* 39 weeks |
| P.E.T. 38 weeks | Abnormal at 38 weeks | Normal 39 weeks Foetal distress | Grossly infarcted | Alive |
| P.E.T. 38 weeks | Abnormal at 38 weeks | Induced 40 weeks Foetal distress | Normal | Alive |
| P.E.T. 36 weeks | Abnormal at 37 weeks | Caesarean section for placenta praevia 38 weeks | Normal | Alive |
| P.E.T. 35 weeks | Abnormal at 38 weeks | Normal 39 weeks Foetal distress | Normal | Alive |

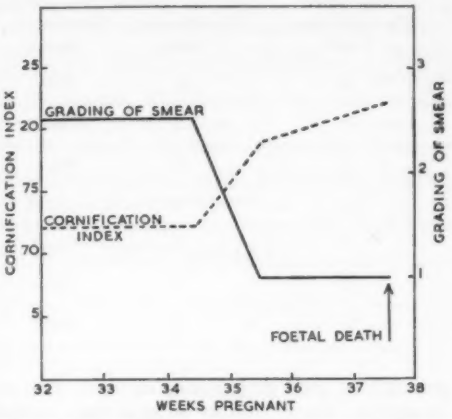
In two patients deterioration of the vaginal smears was observed prior to foetal death.

*Case 1 (Table IV)*

A multigravida with essential hypertension was admitted to hospital in the 32nd week of the pregnancy. During the subsequent four weeks the uterus did not enlarge and in the 37th week of pregnancy proteinuria occurred. Two days later the membranes were ruptured artificially; labour commenced almost immediately following this procedure and its duration was short. There were signs of foetal distress during labour and the infant died one hour after delivery as a result of intra-partum anoxia. Two weeks prior to the expected date of delivery the vaginal smear became abnormal, i.e., the grading of the smear diminished and the cornification index increased (Table V).

TABLE V

*Vaginal Cytology in a Patient with Essential Hypertension —Foetal Death from Intra-partum Anoxia*




Grading of smear diminished and cornification index rose two weeks prior to foetal death.

*Case 2 (Table IV)*

A primigravida, aged 31, with kraurosis vulvae, had a normal smear in the 24th week of pregnancy. Proteinuria and hypertension developed during the 25th week and this continued until the time of the delivery. At the 27th week the cornification index was still normal but the grading of the smear had diminished and the same changes were seen at the 28th week. During the 28th week of pregnancy the foetal heart was not heard and one week after this the foetal death was confirmed by X-ray.

Both these cases demonstrated a change in the vaginal smear two weeks before foetal death; the grading of the smear diminished in both and in one the cornification index increased.

The presence of placental insufficiency was suspected in 2 patients with essential hypertension because the height of the uterine fundus did not increase over a period of several weeks. Vaginal smears remained normal in these patients and subsequently both babies were liveborn; there was no evidence of placental insufficiency.

A comparison between the type of vaginal smear and the characteristics of the pre-eclampsia (Table VI) suggested that abnormal smears were more common when the pre-eclampsia was severe or prolonged. Furthermore, the presence of gross placental infarction or ischaemic villous necrosis in 5 of the 9 patients with abnormal smears suggests that there might be a relationship between placental function and the appearance of the vaginal smear.

## FOETAL DEATH

Vaginal smears were examined before the occurrence of foetal death in 6 patients; four of them had pre-eclamptic toxaemia and have already been mentioned (Table IV); all their smears were abnormal (Fig. 5). Another patient was in hospital throughout pregnancy with severe pyelonephritis; her smear was abnormal from the 32nd until the 36th week when foetal death occurred. A few days later the foetus was stillborn, and histological examination of an infarcted placenta revealed the presence of ischaemic villous necrosis. The sixth patient developed hydramnios during the 37th week of pregnancy, and at this time the vaginal smear was normal. Foetal death occurred during the 38th week and, a few days later, a stillborn foetus with multiple congenital abnormalities was delivered. The placenta was small but otherwise normal, and this finding would be consistent with the presence of a good vaginal smear.

TABLE VI

*The Relation Between the Vaginal Cytology and the Duration and Severity of the Pre-eclamptic Toxaemia*

| Type of Smear | Number of Patients with Pre-eclampsia | Proteinuria | Blood Pressure >160/100 mm. Hg | Pre-eclampsia Longer than 2 Weeks |
|---|---|---|---|---|
| Normal .. .. .. | 21 | 1 | 2 | 2 |
| Abnormal .. .. | 9 | 6 | 7 | 6 |

TABLE VII

*Vaginal Cytology Following Foetal Death* in utero

| Cause of Death | Placenta | Number of Days After Death Smears Taken | Cytology | |
|---|---|---|---|---|
| | | | Cornification Index | Grading of Smear |
| Anoxia (P.E.T.) | No ischaemic necrosis .. .. | 4 | 10 | Poor |
| Anoxia (unknown) | No ischaemic villous necrosis .. | 8 | 5 | Moderate |
| Anoxia (unknown) | No ischaemic villous necrosis .. | 9 | 5 | Poor |
| Anoxia (unknown) | No ischaemic villous necrosis .. | 14 | 3 | Poor |
| Unknown | No ischaemic villous necrosis .. | 35 | 5 | Good |
| Pre-diabetic | Hydropic .. .. .. .. | 2 | 2 | Good |
| Haemolytic disease | Hydropic ischaemic villous necrosis .. | 21 | 3 | Poor |

Smears were also examined in 7 patients following foetal death (Table VII). The appearance of smears taken after foetal death probably depends on the functional state of the placenta at the time of death and its subsequent rate of degeneration. The smears of 3 patients with anoxic stillbirths of unknown cause were graded as poor (Fig. 6), but the worst pregnancy smear occurred in a patient who had suffered from pre-eclamptic toxaemia for several weeks. In 2 patients the smears were normal; one had her second foetal death from an unknown cause and the other had an hydropic placenta associated with pre-diabetes.

## DISCUSSION

Vaginal cytology is a valuable investigation in patients with threatened abortion. When the smear is normal the pregnancy will almost certainly continue, but when the smear is abnormal there is a considerable chance that abortion will occur. Consequently, an abnormal smear may be used as an indication to commence therapy which is thought to prevent abortion. Hochstaedt, Lange and Spira (1960) found abnormal cytology in 118 out of 140 patients with a past history of habitual abortion. In the patients with abnormal smears they found that 78 per cent of their pregnancies survived following progesterone therapy while only 24 per cent of their pregnancies survived with no treatment. These authors suggest that vaginal cytology may be a sensitive and simple guide to the use of hormone therapy in patients with threatened or habitual abortion.

In pre-eclamptic toxaemia and essential hypertension there is an increased risk of foetal death, but at present the obstetrician cannot predict from clinical data when this will occur. From our experience of vaginal cytology in these two conditions it is thought that this investigation may be of value in determining when continued intra-uterine existence will be hazardous to the life of the foetus. The explanation of the occurrence of abnormal cytology in some patients with pre-eclamptic toxaemia is not yet known, but there was some evidence in the present series that an abnormal smear in pre-eclamptic toxaemia may indicate diminished placental function.

## SUMMARY

Endocrine vaginal cytology has been carried out in 116 patients with abnormal pregnancies. Evidence has been produced that this investigation is useful to the obstetrician in determining the prognosis of pregnancies which threaten to miscarry, and also in determining when continued intra-uterine existence will be dangerous for the foetus of patients with pre-eclamptic toxaemia and essential hypertension.

## Acknowledgments

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We are grateful to Schering Berlin for a grant to defray the expense of the coloured plate.

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# ON THE PROBABILITY THAT A WOMAN WHO HAS HAD A SPONTANEOUS ABORTION WILL ABORT IN SUBSEQUENT PREGNANCIES

BY

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THIS paper will examine critically the calculations made first by Malpas (1938) and later revised by Eastman (1956) which state the risk of spontaneous abortion in women with a given number of previous spontaneous abortions. Although scepticism has occasionally been expressed concerning the Malpas and Eastman risks (King, 1953; Reis, 1955; Rakoff, 1959), they have been widely quoted in the literature and are often accepted as "control" figures for studies of preventive therapy in habitual aborters.

Malpas calculated the risk of recurrence by the following method: If $x$ is the percentage of all pregnancies which end in abortion for non-recurrent causes, and $y$ is the percentage of all pregnancies which end in abortion for recurrent causes, then $x+y$ per cent of women will abort in their first pregnancy. Of these, $x.x/100$ (the percentage aborting twice for non-recurrent causes) plus $y$ (the percentage aborting again for recurrent causes) will abort again in their second pregnancy. Similarly, the percentage of these aborting in their third pregnancy will be $(x^2.x/100)+y$, and so on.

The risk of aborting after one abortion is therefore:

$$\frac{\left(\begin{array}{c}\text{per cent of women who abort in}\\ \text{their first two pregnancies}\end{array}\right)}{\left(\begin{array}{c}\text{per cent of women who abort in}\\ \text{their first pregnancy}\end{array}\right)} = \frac{x^2/100+y}{x+y}$$

and after two abortions the risk becomes $\frac{x^3/100+y}{x^2/100+y}$, and so on.

Table I presents the abortion risks after a given number of abortions as calculated by Malpas, and later by Eastman, who used the same method, but chose different estimates of abortion frequency and of the proportion of "habitual" aborters in the general population.

There is no objection to the method of calculation by which these figures were obtained. However, there are objections (1) to the choice of estimates for $x+y$ and $y$, and (2) to the assumptions on which the calculations depend.

### (1) *Choice of Estimates for "$x+y$" and "$y$"*

For "$x+y$" (the frequency of abortion in first pregnancies) Malpas used Whitehouse's (1929) figure of 18 per cent, the percentage of abortions in the 11,430 pregnancies of 3,000 women who attended the Gynaecology Clinic of Birmingham Hospital. Eastman used 10 per cent, the "average" estimate of the frequency of spontaneous abortion from a large series of studies in the literature (see Tietze, 1954).

Both these values are estimates of the overall abortion frequency in the population of pregnant women rather than the estimate for first pregnancies only. These two statistics are not equivalent when there is a tendency for abortions

TABLE I

*Hypothetical Recurrence Risks of Spontaneous Abortion as Calculated by Malpas and Eastman*

| | | Malpas (1938) | Eastman (1956) |
|---|---|---|---|
| Per cent of first pregnancies which abort | $=x+y$ | 18 | 10 |
| Per cent of pregnancies aborting for recurrent causes | $=y$ | 1 | 0·4 |
| Per cent of pregnancies aborting for non-recurrent causes (by subtraction) | $=x$ | 17 | 9·6 |
| | | % | % |
| Calculated risk of abortion after: | | | |
| 1 previous abortion | | 22 | 13 |
| 2 previous abortions | | 38 | 37 |
| 3 previous abortions | | 73 | 84 |

to recur in some women, or when there is an effect of maternal age or parity on abortion frequency (and there is evidence that these tendencies do exist—Stevenson, Dudgeon and McClure, 1959). Moreover, the estimates of overall abortion frequency used are not reliable. Whitehouse's data are biased because they exclude spontaneous abortions not treated in hospital and because they include induced abortions. The 10 per cent "mean" figure used by Eastman is little better, because it is based on data collected from a variety of sources with a variety of biases, so that the mean value depends only on the proportions of estimates which have been included from each source. Estimates of spontaneous abortion frequency have, in fact, ranged from 6 per cent (Randall and Birtch, 1952) to 17 per cent (Tietze and Martin, 1957).

For "$y$" (the frequency of abortion for recurrent causes) Malpas used Whitehouse's figure of 1 per cent for the percentage of women in his sample who had had at least 3 consecutive spontaneous abortions. Eastman used 0·4 per cent, the percentage of women whom Bishop (1937) found to be habitual aborters (defined by Bishop as women with at least 2 consecutive abortions) in a series of reproductive histories taken at Guy's Hospital, London.

The frequency of women who have at least 3 consecutive abortions is not a good measure of the frequency of abortion for recurrent causes, since according to Malpas' own calculations over 20 per cent of such women would have had all their abortions from non-recurrent causes. Also, in Whitehouse's published data, consecutive and non-consecutive abortions cannot be separated, so that the figure of 1 per cent refers to all women of parity zero to 3, who have had 3 abortions, regardless of whether these were consecutive. The figure of 0·4 per cent which Eastman used is even more doubtful, since it refers to women with at least 2 abortions, although Eastman states emphatically that he does not believe such a definition of habitual abortions separates recurrent from non-recurrent causes. Also, it appears from Bishop's paper (which is rather obscure on this point) that his figure is based only on women whose initial 2 or more consecutive abortions were followed by a live-born child!

(2) *Assumptions Underlying the Method of Calculation*

Criticism of the assumptions made by Malpas is more serious than criticism of the estimates used. If the assumptions are valid, insertion of more accurate estimates into the equations could give useful results. If the assumptions are invalid, then the Malpas equations and their results should be abandoned. Although some of their assumptions were not explicitly stated by either Malpas or Eastman, they are clearly a necessary pre-requisite to their algebraic procedures. These assumptions are:

(1) Spontaneous abortions occur either for a "recurrent" cause or for a "non-recurrent" cause.

(2) Women who abort for recurrent causes will do so in the first and all succeeding pregnancies.

(3) After a woman has aborted for a non-recurrent cause, her chances of aborting in a succeeding pregnancy are equal to the frequency of abortion for non-recurrent causes in the population.

Assumption 3 can be questioned in view of the evidence that frequency of spontaneous abortion varies with parity and parental age (Stevenson *et al.*, 1959). Assumption 2 ignores the possibility that a recurrent cause may appear only later in the reproduction period, perhaps after a woman has already had an abortion for a non-recurrent cause.

However, the fundamental error made by Malpas is assumption 1, the idea that causes of abortion can be divided into a group with 100 per cent chance of recurrence, and a group with a chance of recurrence equal to the incidence of abortion (excluding habitual abortion) in the population. The gestation process depends upon such a complex interaction between maternal and foetal factors, both genetic and environmental, that it must be susceptible to interference by a very large number of agents. By analogy with other similar biological problems such as neonatal death, it is likely that, while some of the situations that cause abortion may have a high chance of recurring, and some may have a very low chance of recurring, the majority will lie between the two extremes. There are some types of neonatal death, for instance, where the cause is quite clearly defined, so that the recurrence risks for specific situations can be determined. These risks range from almost zero for some of the deaths from multiple anomalies, such as those caused by maternal infection with rubella, to 25 per cent for lethal recessive conditions, and almost 100 per cent for erythroblastosis foetalis without transfusion therapy when the father is homozygous. Even specific malformations, clinically identical, may have such a spectrum of recurrence risks, depending upon the particular hereditary and environmental factors involved in the case under consideration (Fraser, 1959). There is no reason to believe that the causes of early prenatal deaths are less numerous or less complex than those for neonatal or later deaths. There is evidence, for instance, that some abortions result from maternal-foetal ABO incompatibility (Matsunaga and Itoh, 1958). If this is the cause of abortion in a particular woman, the risk of abortion in the next pregnancy will depend on the genotype of the foetus. Whether the foetus is compatible or incompatible will in turn depend on whether the father is homozygous or heterozygous, and, if he is heterozygous, on which gene is carried in the sperm which fertilizes the egg. This is a cause of abortion where the risk of recurrence falls into neither of Malpas' categories. Almost certainly there are a great variety of such causes, not clearly divisible into "recurrent" and "non-recurrent" categories, and until some evidence to the contrary appears, any calculations based on this subdivision must be regarded as invalid.

It is generally agreed that the frequency of abortions in pregnancies of "habitual" aborters treated by almost any method will be lower than that predicted by Malpas and Eastman (Javert, 1957). Unfortunately this has often been regarded as evidence for the efficacy of a given treatment, or even for the value of some non-specific factor present in *all* therapies. To quote from Mann (1956): "Of primary speculative interest is the observation, well documented in the literature, that almost any type of treatment, in the hands of certain workers, results in success . . . the common factor may well have to do with the therapist's personality." The "common factor" is much more likely to be that the chance of a successful pregnancy without any treatment at all is much higher than these workers realized.

What is needed in place of the "authoritative statistical analyses" (Mann, 1957) of Malpas and Eastman is one good control series to measure empirically just what proportion of habitual aborters *will* abort again without therapy, and whether this risk is, in fact, higher than the risk of a woman with 2, 1, or no previous abortions. Because frequent aborters will seek therapy, and the use of placebos in such a situation raises ethical problems (Rakoff, 1950), such a control series has never been collected, and will probably never be collected.

The use of theoretical calculations of recurrence risks is not an appropriate substitute, however.

An even more undesirable substitute is the previous reproductive histories of the habitual abortion patients being treated with a new therapy (Javert, Finn and Stander, 1949; Davis and Fugo, 1950; Javert, 1957; Rakoff, 1959). Such an estimate of abortion risk without treatment is, of course, quite invalid, since the patients involved were selected precisely because of their bad obstetric history. This fallacy can be most clearly demonstrated by an example. Suppose a group of pregnant women are selected because they have all previously given birth to 2 haemophiliac sons, and no normal sons. Genetic theory predicts that 25 per cent of the resulting babies will be born with haemophilia. If these women are treated with aspirin during the pregnancy, then by the reasoning of Javert and others, one would be forced to the ridiculous conclusion that aspirin during pregnancy had reduced the frequency of haemophilia from 100 per cent (the proportion affected before treatment) to 25 per cent (the proportion affected after treatment).

Probably the best that can be done at present is to collect large series of carefully taken reproductive histories from a representative series of women, and to measure the risk of abortion after a given number of previous abortions. Since some of these pregnancies would have been treated by prophylactic therapy of one sort or another, and some would have been untreated, the estimates derived from such a series would not be ideal by any means. However, they would probably be the best obtainable figures with which to compare the results of any specific therapy, and would certainly be better than those derived from theoretical calculations based on faulty assumptions.

Few studies that can be used for this purpose exist in the literature, and those that have been reported differ in methods of collecting and presenting their data. There is no large series known to the authors where all the abortions concerned were consecutive, and one usually cannot separate consecutive from non-consecutive cases in the data as they are presented. Results from series where no account is taken of whether or not the abortions are consecutive agree that the risk after several abortions is not nearly so high as predicted by Malpas and Eastman. For instance, estimates of the frequency of abortion after three previous abortions are 22 per cent (Tietze *et al.*, 1950), 16 per cent (Rucker, 1952), 11 per cent (Speert, 1954), 21 per cent (Erhardt and Jacobziner, 1956), and 26 per cent (Warburton and Fraser, 1959).

Further data are badly needed concerning the abortion risks for women with particular reproductive histories, especially those with consecutive abortions, so that they can be intelligently advised about their chances of successfully completing pregnancy after several failures.

## Summary

The abortion risks calculated by Malpas and Eastman for women with a given number of previous abortions are based on unreliable estimates of the parameters used and on faulty assumptions underlying the method of calculation. In particular the classification of all causes of abortion into "recurrent" and "non-recurrent" categories is invalid since there is no evidence for such a simple classification, and there is evidence that causes with an intermediate probability of recurrence do exist. The limited data available suggest, too, that the Malpas and Eastman risks are unduly pessimistic.

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# PREGNANCY FOLLOWING ABORTION

BY

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MUCH has been written on the problem of abortion and its incidence (Malpas, 1938; Bevis, 1951, etc.), and it is now generally accepted that if the first pregnancy ends in abortion there is a greater likelihood of abortion occurring in a subsequent pregnancy. Yet after a first abortion most second pregnancies go to the stage of viability. There is little information on whether performance in such "completed" second pregnancies is in any way impaired. Since the incidence of abortion in primigravidae is between 10 and 16 per cent (Stevenson, Dudgeon and McClure, 1959) this is a question of some importance.

The patient in her second pregnancy, the first having ended in abortion, is commonly called a "virtual primigravida". This term suggests that the patient behaves like a primigravida, but, in fact, there is little evidence to show whether or not this is true. In theory some difference might be expected, as a patient who has had an abortion may have a reproductive abnormality which will affect a future pregnancy. The results of an investigation into this problem are reported here.

## METHOD

Three groups of patients were compared: (A) 8,098 primigravidae, (B) 616 second pregnancies, the first one having ended in abortion, (C) 6,505 second pregnancies without previous abortion. The cases constitute all those in the above groups delivered in the City of Aberdeen during the period 1950–1957. They include deliveries in Aberdeen Maternity Hospital, district deliveries, and deliveries in private nursing homes. The history of abortion was given by the patient on routine questioning.

## RESULTS

*Age, height and social class:* Table I shows that group B resembled group C with regard to age; in both, ages tended to be greater than in group A. The height distributions are very similar in all three groups, as are those of social class.

*Threatened abortion and ante-partum haemorrhage:* As shown in Table II, threatened abortion occurred in group B twice as often as in group A, and five times as often as in group C. The incidence of ante-partum haemorrhage was the same in groups A and B, both being higher than in group C.

*Prematurity and perinatal mortality:* Prematurity rate (birth weight 5½ pounds and under) was highest in group B, only slightly less in group A but distinctly less in group C. From further investigation, it became clear that there were no differences of birth weight at any given period of gestation. The increased prematurity rate if significant appeared to be due to the more frequent onset of premature labour and not to the depression of foetal growth.

Perhaps the most striking finding in Table II is the high rate of perinatal death in group B; nearly 50 per cent higher than group A and nearly twice that in group C. Analysis of the perinatal deaths by cause, using the classification of Baird, Walker and Thomson (1954) suggests, despite the small numbers in each category, that the excess mortality in group B is mainly associated with unexplained prematurity and with malformations (Table III).

*Labour and delivery:* The length of labour and type of delivery are analyzed in Table IV. The duration of labour is fairly similar in groups A and B, but all forms of operative

TABLE I

*Distribution by Age, Height and Husband's Social Class*

| | Age % | | | | | Height % | | | | Husband's Social Class % | | | | Total |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | 15–19 | 20–24 | 25–29 | 30+ | | −5′ 1″ | 5′ 1″–5′ 3″ | 5′ 4″+ | | I and II | III | IV and V | | |
| Group B .. | 5·5 | 37·7 | 34·3 | 22·6 | 100·1 | 28·9 | 50·8 | 20·2 | 99·9 | 14·7 | 62·6 | 22·7 | 100·0 | 616 |
| Group A .. | 11·6 | 49·8 | 27·5 | 11·2 | 100·1 | 28·7 | 49·2 | 22·1 | 100·0 | 14·3 | 62·9 | 22·8 | 100·0 | 8,098 |
| Group C .. | 2·2 | 32·6 | 37·4 | 27·8 | 100·0 | 28·9 | 49·0 | 22·1 | 100·0 | 14·1 | 60·0 | 25·9 | 100·0 | 6,505 |

TABLE II

*Obstetric Performance*
(numbers of cases in brackets)

| | Threatened Abortion % | Ante-partum Haemorrhage % | Prematurity % | Perinatal Deaths per 1,000 | Total |
|---|---|---|---|---|---|
| Group B .. .. | (35) 5·7 | (16) 2·6 | (51) 8·3 | (26) 42·2 | 616 |
| Group A .. .. | (209) 2·6 | (212) 2·6 | (619) 7·6 | (250) 30·9 | 8,098 |
| Group C .. .. | (75) 1·2 | (109) 1·7 | (332) 5·1 | (154) 23·7 | 6,505 |

TABLE III

*Perinatal Mortality by Cause*
(numbers of cases in brackets)

| | Premature Unknown | Mature Unknown | Ante-partum Haemorrhage | Toxaemia | Trauma | Deformity | Other | Total | Rate/1,000 |
|---|---|---|---|---|---|---|---|---|---|
| Group B .. | (7) 11·4 | (3) 4·9 | (1) 1·6 | (4) 6·5 | — — | (7) 11·4 | (4) 6·5 | 26 | 42·2 |
| Group A .. | (62) 7·7 | (35) 4·3 | (25) 3·1 | (34) 4·2 | (36) 4·4 | (35) 4·3 | (23) 2·8 | 250 | 30·9 |
| Group C .. | (44) 6·8 | (24) 3·7 | (23) 3·5 | (8) 1·2 | (17) 2·6 | (27) 4·2 | (11) 1·7 | 154 | 23·7 |

TABLE IV

*Method of Delivery and Length of Labour*

| | Method of Delivery % | | | | | Length of Labour % | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | Caesarean Section | Forceps | Assisted | Spontaneous | | −6 Hours | −12 Hours | −24 Hours | 24+ Hours | |
| Group B | 6·5 | 19·2 | 3·1 | 71·3 | 100·1 | 19·6 | 30·8 | 34·9 | 14·6 | 99·9 |
| Group A | 4·0 | 16·1 | 1·8 | 78·0 | 99·9 | 16·2 | 34·3 | 33·5 | 16·0 | 100·0 |
| Group C | 2·3 | 2·0 | 1·0 | 94·8 | 100·1 | 39·7 | 36·8 | 20·0 | 3·5 | 100·0 |

delivery are slightly more frequent in group B. In group C labours are naturally much shorter and more often unassisted because of the stretching of the birth canal in the first labour.

## Discussion

Details of obstetric history in maternity case records are not always reliable. For this reason the accuracy of the diagnosis in every case of abortion in this study cannot be guaranteed. In some the amenorrhoea might have been due to a temporary endocrine disturbance. Again it is possible that some very early abortions may not have been recorded. The error from these causes is thought to be small.

The high incidence of threatened abortion and premature labour in the second pregnancies of patients who had previously had an abortion suggests a common aetiology, one which stimulates the premature onset of uterine contractions, but the incidence of ante-partum haemorrhage is the same in groups A and B, which both have a slightly higher incidence than group C. This may suggest that threatened abortion and ante-partum haemorrhage have different aetiologies. The small increase in all types of assisted delivery in group B is probably explained by the attitude of the obstetrician. In the virtual primigravida he is likely to undertake Caesarean section and forceps delivery more readily especially for such conditions as foetal distress and prolonged labour.

It has been shown in Table II that the perinatal mortality in group C (second pregnancies) is distinctly less than in group A (first pregnancies). This is in line with the usual experience that death rates are relatively high in a first pregnancy and lowest in the second. The death rate in group B (virtual primigravidae) is one third higher than in group A. Table III gives an analysis of the causes of death by cause in an attempt to explain the difference. Numbers are too small to give statistically significant results, but they suggest that death rates in group B are higher from all causes except birth trauma than in group A. The absence of deaths from trauma in group B may be associated with the increased number of Caesarean sections and the tendency to avoid any chance of traumatic delivery in view of the obstetric history.

As already noted, there is a suggestion (not statistically significant) that the death rates from prematurity and from malformation are particularly high. It is well known that in a large percentage of cases of abortion the foetus is abnormal. Stevenson, Dudgeon and McClure (1959) found that 26 out of 84 foetuses (31 per cent) were deformed to the naked eye, and Hertig and Rock (1949) found that 12 of 28 very early ova (43 per cent) were abnormal on microscopic examination. It is tempting to suggest that some maternal or paternal factor may be particularly liable to cause foetal malformation in certain individuals. This factor may result in abortion in the first pregnancy and in the second may cause a malformed stillbirth. Turnbull and Walker (1956) discussed the effect of threatened abortion on the outcome of pregnancy, and showed that the incidence of deformity following threatened abortion was 10·6/1,000, which is probably significantly higher than the average. Only one of the deformity group in this series had a history of threatened abortion.

As far as is known the only "advantage" conferred by abortion in a first pregnancy is a decreased liability to pre-eclampsia in the second pregnancy (MacGillivray, 1958). He showed that the risk of severe pre-eclampsia is reduced by two-thirds and that of mild pre-eclampsia by one-third in second pregnancies where the first was of short duration. In this series, however, there is no decrease attributable to pre-eclampsia in group B. This is likely to be a chance effect of small numbers.

## Summary

Patients who start their reproductive life with an abortion have an increased risk of threatened abortion and perinatal death in their second pregnancies. Labour resembles that of primigravidae.

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# INCOMPETENCE OF THE INTERNAL OS

## Report of a Case

BY

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IN recent years "cervical incompetence" or "insufficiency of the internal os" has come to be recognized as one of the important and curable causes of habitual abortion or multiple miscarriage.

### AETIOLOGY

Danforth (1947) of Chicago showed that, as a result of congenital defect, trauma by dilators, forceps extraction or the passage of a large infant, the fibro-muscular junction between the isthmus uteri and the histological internal os might be unable to retain the growing foetus in the uterus. The same situation can arise with high amputation in a Fothergill operation.

### DIAGNOSIS

Clinically, such a condition may be suspected in patients who abort repeatedly at a stage in pregnancy which will vary according to the degree of cervical impairment present. The abortions characteristically occur in the second trimester and are usually preceded by bulging or painless rupture of the membranes. The diagnosis can be made in a non-pregnant uterus in two ways. First, a special hysterogram can be carried out, using a cannula tipped with an inflatable bulb. This is inserted into the uterine cavity and lipiodol or other radio-opaque substance injected so as to distend the bulb. Then with gentle traction on the cannula, an X-ray plate is taken in the lateral and antero-posterior positions. This will demonstrate an abnormally patulous internal os. In a typical case, an internal os of over 10 mm. is usually demonstrable, a criterion first established by Palmer and Lacomme (1948). On the other hand, it may be possible, with the non-pregnant patient anaesthetized and in the lithotomy position, to pass a Hegar dilator of size 4 or larger into the uterine cavity without any difficulty (Green-Armytage and McClure Browne, 1957).

Asplund (1952) and Dorangeon (1956) state that the cervical canal is widest in the proliferative phase of the menstrual cycle, when it averages 6 mm.; in cases of cervical incompetence, the internal os will easily admit a dilator of at least 8 mm. diameter (Hegar size 8), often without an anaesthetic. During pregnancy it is essential that stringent diagnostic criteria should be fulfilled before any operative treatment is contemplated.

Shirodkar (1953) described in his preliminary study of 15 cases of habitual abortions, the following criteria for the diagnosis of incompetence of the internal os. There is a gradual passive dilatation of the cervix in the second trimester of pregnancy. Membranes can either be felt through the dilated cervix or even a bag of membranes may be projecting into the vagina. There are no labour pains. He continues further that the condition occurs between four and a half to seven months and you may get cases with as many as eight to nine abortions.

In those cases in which the first evidence of impending abortion is premature rupture of membranes, it is tempting to assume, as do Green-Armytage and McClure Brown (1957)

and many before them, that an incompetent cervix is the cause. But Jeffcoate and Wilson (1956), in a controlled study of cases of abortion and premature labour, showed that the patients with radiologically demonstrated cervical deficiency are not more likely to commence labour in this way than in any other. According to them, a history of the membranes rupturing before the onset of expulsive uterine contractions is without significance in this context. The nearest approach to the diagnosis is a well-authenticated history of several abortions occurring after the fourteenth week, the foetus being alive at birth and the process of expulsion being characterized by painless dilatation of the cervix, associated with a hysterographic evidence of a funnel-shaped cervix between pregnancies.

## Treatment

Various operations on the cervix have been performed to cure the insufficiency of the internal os. Lash and Lash (1950) drew particular attention to the defects of the cervical canal resulting from obstetrical and gynaecological trauma and described a method for its repair.

After reflecting the bladder from the anterior wall of the cervix, mattress sutures are applied on the anterior wall picking up cervical tissue on either side of the midline. Shirodkar (1953), however, realizing that the defect in the internal os could be, and most frequently was, in a situation other than anterior, described a method of encirclement by means of a fascial strip (fascia lata), forming a "purse-string" around the internal os. In recent years the Shirodkar operation has been performed in its original form or with minor modifications with very successful and encouraging results. Materials like nylon tape, nylon thread 7N or 8N, kangaroo tendon, Mersilk No. 4, silver and tantalum wires have been employed in place of fascia lata to achieve similar results. Barter *et al.* (1958) have suggested synthetic fine mesh Dacron, and Page (1958) advocates the production of a fibrous stricture from reaction to thick catgut and talc powder. Ian MacDonald (1957) has described a technique of applying a "purse-string" suture without incising the mucous membrane. A "purse-string" suture of No. 4 Mersilk on a Mayo needle is inserted around the exocervix as near as possible to the level of the internal os. The results have been equally successful. Operations on the cervix undoubtedly have a place in therapy; but to employ them in cases insufficiently investigated and unproved is dangerous and may discredit an ingenious procedure.

## Case History

On 12th March, 1959, Mrs. S., aged 29, was referred because of 9 premature labours between 1949 and 1958, all ending between 28 and 32 weeks. The first baby, delivered at 32 weeks, weighed two pounds fifteen ounces. It was the heaviest of the series and survived following care in the premature baby unit for ten weeks. The next 6 infants died of prematurity and infection. Her eighth baby, born in 1956, again at 32 weeks, weighed two pounds four ounces and survived after twelve weeks care in the premature baby unit. Her next baby weighed two pounds six ounces. It died on the ninth postnatal day of prematurity and acute bilateral broncho-pneumonia. She had been given progesterone implants during both of these pregnancies in 1956 and 1958.

She had scarlet fever and rheumatic fever at the age of fourteen years. She had appendicectomy in 1946.

### *Antenatal Notes*

She was a healthy-looking multigravida. General examination revealed no abnormality. Her blood group was A, Rhesus positive, and both the Wassermann and the Kahn reactions were negative. She was found to be fourteen weeks pregnant and her expected date of delivery was 11th September, 1960. Speculum examination at that stage did not reveal any abnormality of the cervix. She attended the clinic after four weeks when a provisional diagnosis of cervical incompetence was made. The cervical canal was funnel-shaped; the external os just admitted the tip of the index finger. It was decided to re-assess her in the next few weeks to confirm the diagnosis of cervical incompetence. On 11th May, 1959, when she was twenty-two weeks pregnant, the

external os admitted one finger easily and the membranes were bulging into the upper end of the cervical canal. A purse-string suture (MacDonald, 1957) of double Mersilk No. 4 was inserted around the cervix as near as possible to the level of the internal os and the patient was sent home on the fifth post-operative day. Following that, she attended the clinic at regular intervals. The foetus presented by the breech at the 28th week, but had undergone spontaneous version to vertex presentation by the 32nd week. The highest blood pressure recorded was 130/80 and no abnormal constituents were found in the urine at any time. The fundus of the uterus at all times had corresponded to the duration of pregnancy. When examined at the 36th week, the vertex presented (L.O.A.) and the head was freely mobile above the pelvic brim. A pelvic assessment done at that stage revealed the pelvis to be of gynaecoid shape.

She was admitted in early labour at thirty-seven weeks on 20th August, 1959. Vaginal examination revealed that the foetal head had entered the brim and that the cervix was completely effaced and thinned out above the MacDonald suture. The knot of the purse-string suture, which seemed buried in the cervix, was gently pulled out, snipped and the thread removed. The cervix, which barely admitted a finger tip, dilated to two fingers and the membranes started bulging through the dilating os. After a temporary quiescence of about twelve hours, labour commenced suddenly at 11.30 a.m. on the day following admission. At 1.30 p.m. the membranes ruptured. At 1.35 p.m. a live male infant was delivered normally. The baby cried lustily and weighed six pounds two ounces. Her puerperium was uneventful. The baby was artificially fed and, when discharged on the 14th puerperal day, had regained its birth weight. At the postnatal examination six weeks after delivery both were well. The baby now weighed seven pounds eight ounces.

Involution of all the maternal pelvic organs was complete and no abnormality was detected.

## Summary

A case of habitual miscarriage, in which the woman had lost seven babies out of nine pregnancies, was carried through to a successful pregnancy after encircling the exocervix with double Mersilk (MacDonald's method). Incompetence of the cervix was confirmed during the antenatal period (at twenty-second week) when the cervical canal was felt to be funnel-shaped and one finger dilated, with membranes bulging. She started labour spontaneously at thirty-seven weeks after extraction of the stitch and was delivered vaginally and successfully.

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# UNEXPLAINED PREMATURITY: INVESTIGATION OF POSSIBLE CAUSES

BY

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IT is usually accepted that prematurity has no apparent cause in approximately half of the cases and the literature contains very few reports of investigations into possible causal factors in this large group. In the present series of 542 cases occurring over a four-year period, the total of unexplained prematures was 52 per cent. These cases are unlikely to form a homogeneous group and it was therefore decided to examine them in detail with particular reference to the parity of the mother and to the previous and subsequent obstetric histories, to find out whether there were any recognizable types or patterns of occurrence.

TABLE I
*Order of Parity*

| 1st | 2nd | 3rd | 4th | 5th | 6th |
|---|---|---|---|---|---|
| 135 | 70 | 40 | 16 | 8 | 14 |

Figure 1 shows the distribution of cases according to parity and Table I the order of parity. Table II gives the comparative figures for the "Known Causes" group in the same four-year period. The larger number of "Known Cause" prematures in the multiparae is due to the higher incidence among multiparae of antepartum haemorrhage, twin pregnancy, foetal deformity and erythroblastosis.

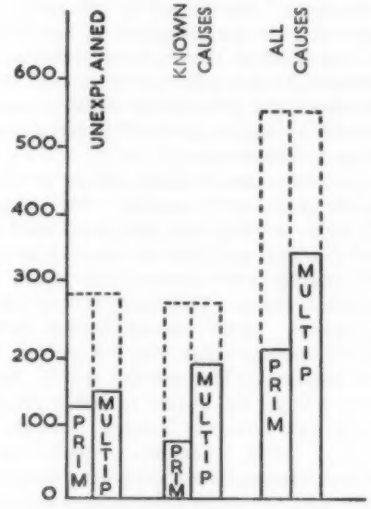


FIG. 1
Ratios of primiparae to multiparae.

## UNEXPLAINED PREMATURES: PRIMIPARAE

There were 130 cases, 40 being apparently under 36 weeks duration and the overall perinatal mortality was 27 cases (21 per cent). The following general factors were present:

(*a*) Mean height of mothers was 5 feet 1 inch.

(*b*) Illegitimate rate was 16 per cent, as compared to 5·1 per cent for Scotland and 6·5 per cent for Dundee.

This high figure is possibly related to social class although no social class details were available in the records.

TABLE II

*Known Causes of Prematurity*

| | Primi-parae | Multi-parae | Total |
|---|---|---|---|
| Accidental haemorrhage | 11 | 39 | 50 |
| Placenta praevia | 2 | 19 | 21 |
| Twins | 18 | 44 | 62 |
| Toxaemia | 31 | 29 | 60 |
| Deformity | 12 | 28 | 40 |
| Rh. factor, etc. | 2 | 24 | 26 |
| Total | 76 | 183 | 259 |
| Unexplained | 135 | 148 | 283 |

The following obstetric factors were present:

| | *Cases* |
|---|---|
| (1) Threatened abortion | 11 |
| (2) Ante-partum bleeding not otherwise counted | 9 |
| (3) Severe pre-eclampsia (not induced) | 10 |
| (4) External version followed by onset of labour | 2 |
| (5) Fibroids | 2 |
| (6) Membranes stripped, mistaken dates | 2 |
| Total | 36 |

*Follow-up of Primiparae*

Fifty-four of the 135 women were traced in a subsequent pregnancy, 33 being untraced and 48 having had no further pregnancy to date.

Table III shows that the remaining 54 produced in the second pregnancy 43 full-time and 11 premature infants. Where the first pregnancy was apparently a true early labour, 5 out of 19 (over 20 per cent) produced a second premature baby. Where the first pregnancy was a small baby at term, only 6 out of 35 have produced a second premature baby.

## OBSTETRIC HISTORY OF MULTIPARAE

*Recurrent Prematurity*

Table IV shows the previous history of the 70 cases where unexplained prematurity occurred in a second pregnancy, 38 of them being apparently small babies at term and 32 being delivered a month or more from term.

Of the 38 full-time cases, the present premature baby followed a premature baby in 15 cases and a mature baby in 23 cases. Comparison of the weights of the two babies in these 23 cases showed a difference of 1 pound or less in 12 cases, 1 pound to 1½ pounds in a further 7 cases,

TABLE III

*Subsequent History of Primiparae—54 Cases*

| | Under 36 Weeks | | Over 36 Weeks | |
|---|---|---|---|---|
| 1st pregnancy | 19 | | 35 | |
| | Full Term | Premature | Full Term | Premature |
| 2nd baby | 14 | 5 | 29 | 6 |

Total

Full Term 43 Premature 11

TABLE IV

*Previous History of Second Parae—70 Cases*

| | Under 36 Weeks | | Over 36 Weeks | |
|---|---|---|---|---|
| 2nd pregnancy | 32 | | 38 | |
| | Full Term | Premature | Full Term | Premature |
| 1st pregnancy | 22 | 10 | 23 | 15 |
| Deaths in 2nd pregnancy | 10 | 2 | 0 | 0 |

while in the remaining 3 the difference was over 1½ pounds and up to 4 pounds. In other words, the majority, 19 out of 23 cases, have produced two babies of almost the same weight, the first being just under and the second just over the 5½ pounds mark. The remaining 4 cases showing a considerable drop in weight of the second baby all had severe pre-eclampsia, not included in the "Known Causes" group because labour was not induced. It is also noted that there were no deaths in this group of 23 cases, the babies being all approximately 5 pounds in weight.

In the 15 cases where both babies were premature by weight, but the second was at term, only 5 were under 5 pounds and none under 4¾ pounds, 10 were larger than their predecessor though still under 5½ pounds and only 2 were smaller but only by 1 pound and 1¾ pounds. There were no deaths in the 15 cases.

*Isolated Prematurity*

Of the 32 cases which were early small babies, under 36 weeks, 22 cases followed a previous full-time pregnancy and here the weight difference in the 2 babies was very much more marked, figures of 2½–4½ pounds being frequent, e.g., 7 pounds 12 ounces–4 pounds 12 ounces; 7 pounds 2 ounces–3 pounds; 7 pounds–4 pounds 4 ounces. No explanation can be found for all of these 22 cases but the following factors were present.

| | *Cases* |
|---|---|
| (1) Abortion between pregnancies .. | 6 |
| (2) Threatened abortion in second pregnancy .. .. .. | 4 |
| (3) Ante-partum bleeding, unclassified | 3 |
| (4) Severe pre-eclampsia with albuminuria .. .. .. .. | 2 |

The mortality in this group, which contained the smallest babies was of course very high, 10 out of 22.

The remainder of the multiparae who had a previous small early baby followed by a second early small baby, 10 cases with 2 deaths, had amongst them 3 women who can best be described as "Habituals", i.e., they had produced several abortions and several premature; and also 2 women who had slight unclassified ante-partum bleeding.

PREMATURITY IN THIRD PREGNANCY

In 40 cases "Unexplained" prematurity occurred in the third pregnancy (Table V) and of these 27 were apparently early babies and 13 were small babies at term. In the latter group, the previous two pregnancies had been 2 full-time in 8 cases, 2 prematures in 1 case and 1 full-time and 1 premature in 4 cases. In the other 27 cases the figures for the preceding pregnancies were: 2 full-time in 15 cases, 2 prematures in 5 cases, 1 full-time and 1 premature in 7 cases. That is to say, prematurity occurred as an isolated incident after two normal pregnancies in 23 out of 40 cases, suggesting the operation of a factor peculiar to that pregnancy. In these the following factors were present, slight ante-partum bleeding in 6 cases, severe toxaemia in 1, acute febrile illness in 2, uterine deformity in 1 case. At the opposite end of the scale, prematurity followed 2 previous prematures in 6 cases and of these 2 had uterine deformity, 1 was a case of habitual abortion and 1 had had 2 macerated prematures. In the 11 cases with a mixed previous history, 2 had ante-partum bleeding and 2 had uterine deformities.

TABLE V

*Previous History of "Third Pregnancy Prematures"—40 Cases*

| | Under 36 Weeks | | | Over 36 Weeks | | |
|---|---|---|---|---|---|---|
| 3rd pregnancy .. .. | 27 | | | 13 | | |
| Previous pregnancies .. | 2 Full Term 15 | 2 Premature 5 | Full Term +Premature 7 | 2 Full Term 8 | 2 Premature 1 | Full Term +Premature 4 |

| Totals | | | | | |
|---|---|---|---|---|---|
| 2 full term .. | 23 | 2 premature .. | 6 | 1 full term+1 premature .. | 11 |

The higher parities contributed too few cases and were not analyzed.

### "Habitual Prematurity"

Finally there was a group of 10 women who in addition to producing 24 of the 283 unexplained prematures in this series, have produced a further 15 prematures and 15 abortions as well as 5 full-time babies. Hysterography was carried out on several of these "Habituals" and of 7 cases so far investigated (one being pregnant, one untraced and one unwilling to come) 3 have normal uteri, 3 have various degrees of bicornuate uterus and 1 has a unicornuate uterus. In a further 11 unselected cases in the series, hysterography revealed 2 with bicornuate uterus. The "Incompetent cervix" syndrome was not looked for in those patients X-rayed but there does not seem to be any reason why this mechanism should not operate at 28 weeks as well as at 20 weeks and further investigation might be profitable particularly where a large baby is followed by a very early premature baby.

### Discussion

Various factors, including maternal age, birth spacing, antenatal care, nutrition, etc., appear to influence the occurrence of prematurity and there seems no doubt that Social Class has a definite relation to the incidence of prematurity. Much of the information available, however, is very contradictory and it is difficult to understand why these general influences should operate in one pregnancy and not in the next as, for example, in those cases with marked weight differences in the two pregnancies.

The present small survey does not produce any very definite new information but appears to confirm that there are two types of unexplained prematurity: (*a*) the small baby at term, and (*b*) an early small baby due to the spontaneous onset of premature labour often with early rupture of membranes. With regard to the first group, it would seem that there may be a genetic factor which is responsible for small women, as many of them are producing small babies, and there may also be a nutritional factor. There may be in addition the effect of continuing employment during late pregnancy which is common in the jute industry in this area.

It is more difficult to explain those cases with a marked weight drop in the second baby. There are some women who seem unable to produce other than small babies but there are many in whom prematurity is an isolated occurrence.

A large-scale statistical investigation of the problem would probably reveal more definite information as to possible causal factors in these otherwise unexplained prematures.

The part played by anatomical factors such as uterine deformity or incompetent cervix is difficult to estimate. Fundal abnormalities are by no means uncommon and are known to be associated with a high incidence of abortion and premature labour as well as breech and transverse presentations and retained placenta. Many of them, however, have a perfectly normal obstetric history in spite of gross deformity and some even are associated with postmaturity. Incompetence of the cervix, however, might well explain many of the very early cases.

### Prognosis

The outlook for a primipara who has a premature baby seems to be fairly good especially if the pregnancy has gone beyond 36 weeks. The greatest foetal wastage occurs in those patients who have a very early small baby following a normal sized baby.

### Summary

A survey of a small series of unexplained premature infants has been made. A suggestion is made for further investigation of anatomical factors and examination of a much larger series.

# HYDRAMNIOS AND ASSOCIATED MATERNAL AND FOETAL COMPLICATIONS

BY

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DURING the period 1950–1958 inclusive there were 15,967 confinements in the Area Department beds of United Oxford Hospitals. In the summaries of the case sheets a mention of hydramnios occurred 194 times. The diagnosis involved 181 women as nine of them had had hydramnios in two and two had hydramnios in three pregnancies.

On scrutiny of the original antenatal and labour records without reference to the outcome of the pregnancy, the evidence as recorded for one or more hydramnios did not seem to us sufficient to support the diagnosis in 35 cases. In all of these hydramnios had been diagnosed in only one pregnancy. In all probability the diagnosis was correct in at least some of these cases but inadequate case records did not justify the inclusion of any of these 35 patients in this series.

An attempt was made to trace the remaining 146 women. One hundred and twenty-one women were traced but seven were not visited. The reasons for this were that two were not married, one had died, and four did not wish to co-operate. The 25 untraced patients were mostly wives of service men who had been stationed near Oxford in the early years of the period studied. Some others were dwellers in caravan sites or in hutted camps since demolished.

In all there were visited 114 women who had had 132 pregnancies complicated by hydramnios. Including the patients not visited the rate of hydramnios per pregnancy in the hospital series is about 0·9 per cent. This is within the range of other frequencies reported in England and Wales but is lower than that reported for Belfast (Stevenson, 1960) or Dublin (Barry, 1958). One of us (A.C.S.) has seen the original case sheets from both the Oxford and Northern Ireland series and finds it difficult to believe that the standard of acceptance in the two series was substantially different.

It seems superfluous to discuss here the difficulties of laying down diagnostic criteria of hydramnios which could be followed in clinical practice. These have probably deterred many from attempting to assess the extent of the foetal hazard in association with hydramnios. Published data are relatively scanty in respect of this complication of pregnancy, however it is defined, although it has such a high association with foetal malformations. The problem is considered by Stevenson (1960).

We accepted the clinical diagnosis as recorded in the antenatal period when it was substantiated by an excessive amount of liquor (over 40 fluid ounces) at the time either of spontaneous or artificial rupture of the membranes.

TABLE

*Maternal Age by Pregnancy Order in 114 Index Pregnancies Complicated by Hydramnios with Comparative Figures for the Hospital Series from Which They were Derived*

| Maternal Age (Years) | Pregnancy Order | | | | | | | | | | | | % of Total in Series | Confinements in Hospital Over Period | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | 11 | Total | | No. | % |
| 15– | 6 | – | – | – | – | – | – | – | – | – | – | 6 | 5·3 | 879 | 5·5 |
| 20– | 19 | 3 | 1 | 3 | – | – | – | – | – | – | – | 26 | 22·8 | 4,735 | 29·7 |
| 25– | 12 | 8 | 4 | 6 | 2 | – | – | – | – | – | – | 32 | 28·1 | 4,766 | 29·8 |
| 30– | 7 | 5 | 4 | 4 | 3 | – | – | – | 1 | – | – | 24 | 21·1 | 3,162 | 19·8 |
| 35– | 8 | – | 4 | 7 | 1 | 1 | – | – | – | – | 1 | 22 | 19·3 | 1,736 | 10·9 |
| 40+ | – | – | – | 1 | 2 | – | – | – | – | – | 1 | 4 | 3·5 | 689 | 4·3 |
| Total | 52 | 16 | 13 | 21 | 8 | 1 | – | – | 1 | – | 2 | 114 | 100 | 15,967 | 100 |
| Total in Series (%) | 45·6 | 14·0 | 11·4 | 18·4 | 7·0 | 0·9 | – | – | 0·9 | – | 1·8 | 100 | | | |
| Confinements in hospital over period — No. | 8,941 | | | | | 7,014 | | | | | | 15,955* | | | |
| Confinements in hospital over period — % | 56·0 | | | | | 44·0 | | | | | | 100 | | | |

* Excludes 12 where parity was not recorded.

## THE DATA

When considering the many variables associated with reproductive history, the relevant pregnancy, the labour and delivery and the fate of the conceptus, it is always difficult to show all the relationships in which readers might be interested. Protocols for the characterized pregnancies and for the pregnancy histories of the mothers concerned are, however, available. Stencil copies will be sent on request to anyone who wishes to study relationships not set out in this paper. Stencil copies are also available of details of each malformed foetus or child.

Each mother was visited and questioned and whenever possible records of hospital confinements were consulted.

## PARENTAL AGE AND PREGNANCY ORDER

Paternal age does not appear to be related. Table I enables the relationship with maternal age and pregnancy order to be assessed, in comparison with the distribution of first and subsequent pregnancies in the 15,967 pregnancies in hospital from which the series was derived. Maternal age distributions are very similar for the hydramnios complicated and other pregnancies.

In the data as tabulated there is a significant deficiency of first births in the hydramnios cases ($\chi^2=4{\cdot}65$, df=1, $0{\cdot}05>P>0{\cdot}02$). This is not a proper comparison, however, as for practical purposes all cases of hydramnios are admitted to hospital while there is a particularly highly selected intake of primigravidae in Oxford.

## RECURRENCE OF HYDRAMNIOS IN SUBSEQUENT PREGNANCIES

Of the 114 women in this series 14 had two pregnancies complicated by hydramnios and two had three such pregnancies. It is difficult to estimate with confidence the risk of repeat frequency because these women no doubt have completed varying proportions of their pregnancy histories. In all these 114 women had 387 pregnancies. Of those not complicated by hydramnios 34 were abortions (so early that hydramnios would not have been diagnosed). If these abortions and one hydramnios pregnancy in each mother are ignored, there were 239 other pregnancies and of these 18 (7·5 per cent) were complicated by hydramnios. There seems little doubt, therefore, of the aggregation of cases in pregnancies in the same patient. These 114 women had 83 pregnancies which occurred *subsequent* to the first hydramnios pregnancy but then of these 10 were abortions and did not continue until hydramnios would be likely to be diagnosed. Again, ignoring the abortions the frequency in the subsequent pregnancies was 18/73 or 24·7 per cent. It is, perhaps, noteworthy, that (1) both women having had three hydramnios pregnancies had them in successive pregnancies (1, 2, 3 and 2, 3,

TABLE II

*Outcome of 132 Pregnancies (in 114 Women) Complicated by Hydramnios*

| | Single Births | | | Twin Births | | | | | Total | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | Male | Female | Total | Male/ Male | Male/ Female | | Female/ Female | Total | Male | Female | Total |
| | | | | Male | Male | Female | Female | | | | |
| LB (A) | | | | | | | | | | | |
| Normal .. | 28 | 29 | 57 | 10 | 6 | 5 | 4 | 25 | 44 | 38 | 82 |
| Malformed .. | — | 1 | 1 | 2 | — | 1 | — | 3 | 2 | 2 | 4 |
| Total .. .. | 28 | 30 | 58 | 12 | 6 | 6 | 4 | 28 | 46 | 40 | 86 |
| LB (D) | | | | | | | | | | | |
| Normal .. | — | 1 | 1 | 1 | 1 | 2 | — | 4 | 2 | 3 | 5 |
| Malformed .. | 4 | 7 | 11 | — | — | — | — | — | 4 | 7 | 11 |
| Total .. .. | 4 | 8 | 12 | 1 | 1 | 2 | — | 4 | 6 | 10 | 16 |
| SB | | | | | | | | | | | |
| Normal .. | 3 | 5 | 8 | 7 | — | — | 6 | 13 | 10 | 11 | 21 |
| Malformed .. | 10 | 21 | 31 | — | 1 | — | — | 1 | 11 | 21 | 32 |
| Total .. .. | 13 | 26 | 39 | 7 | 1 | — | 6 | 14 | 21 | 32 | 53 |
| Total .. .. | 45 | 64 | 109 | 20 | 8 | 8 | 10 | 46 | 73 | 82 | 155 |

No. of mothers 114 No. of pregnancies 132 No. of offsprings 155
LB (A) = Liveborn and still alive LB (D) = Liveborn but died SB = Stillborn

4), (2) of the fourteen women who had two such pregnancies eleven had them in successive pregnancies and six of them were affected in the first two pregnancies. Only three women had had uncomplicated pregnancies subsequent to a second complicated by hydramnios.

The significance of this is also difficult to assess and can only be illuminated by following up a series of women until the end of reproductive life.

## Condition of the Offspring of Pregnancies Complicated by Hydramnios

This information is summarized in Table II.

The 132 pregnancies complicated by hydramnios resulted in 109 single births and 23 twin pairs. This frequency of twin births 23/132 or 17·42 per cent may be compared with the frequency of twin births in the hospital over the period 1950–1958 or 357 in 15,967 or 2·24 per cent or excluding the hydramnios cases 2·11 per cent. It may also be noted that of the 23 twin pairs 15 (65·2 per cent) were of like sex twins. This is about the expected figures for all births, e.g., in England and Wales in 1949–1950 there were 16,870 pairs of twin births when at least one twin was born alive; of these 10,791 or 63·4 per cent were of like sex twins.

These findings support those in other series of a high rate of twins associated with hydramnios. There is, however, no evidence in this series that the excess is determined mainly by monozygotic twins. This is rather in conflict with a view not uncommonly expressed that the complication is almost confined to monozygotic twins (Browne and Browne, 1955).

### *Stillbirth, Early Death and Malformation*

It will be seen that of 109 single births 43 (39·4 per cent) were malformed and that of those not malformed 9 were stillborn or died before leaving hospital, a total early death plus malformation rate of 47·7 per cent. Of the 46 twin births, 4 (8·7 per cent) were malformed and 17 (37·0 per cent) were stillborn or died early. In all, therefore, 45·7 per cent were lost or were malformed.

This malformation frequency is not significantly different from half that in single births. There is a suggestion of increased perinatal non-malformed frequency per child in twins relative to single births in this series as in the Belfast data. It is in all probability a reflection of the almost constant occurrence of hydramnios in only one sac. The other wastage is presumably a reflection of the general hazards of twin pregnancy and delivery.

Table III shows the types of these 47 malformations. As will be noted 27 of them are anencephaly with a 2 : 1 preponderance in females, whereas the sex proportion in the

TABLE III

*Types of Malformations Noted in the Offspring of Pregnancies Complicated by Hydramnios*

| Malformation | Males | | | | Females | | | | Total |
|---|---|---|---|---|---|---|---|---|---|
| | LB* (A) | LB (D) | SB | Total | LB (A) | LB (D) | SB | Total | |
| Anencephaly only | – | – | 3 | 3 | – | – | 9 | 9 | 12 |
| Anencephaly, spina bifida and/or other malformations | – | – | 5 | 5 | – | – | 10 | 10 | 15 |
| Hydrocephaly, types unknown (head perforated) | – | – | 1 | 1 | – | – | – | – | 1 |
| Arnold-Chiari malformation | – | – | – | – | – | 1 | – | 1 | 1 |
| Lumbo-sacral spina bifida | – | – | – | – | – | – | 1 | 1 | 1 |
| Pyloric stenosis (pair of twins) | 2 | – | – | 2 | – | – | – | – | 2 |
| Cerebral agenesis—talipes | – | – | – | – | – | 1 | – | 1 | 1 |
| Atresia of oesophagus | – | 1 | – | 1 | – | – | – | – | 1 |
| Tracheo-oesophageal fistula | – | 1 | – | 1 | – | – | – | – | 1 |
| Volvulus | – | – | – | – | – | 1 | – | – | 1 |
| Large sub-mental swelling | – | – | – | – | – | 1 | – | 1 | 1 |
| Absent thumbs | – | – | – | – | – | – | 1 | 1 | 1 |
| Ventricular septal defect, pulmonary stenosis, webbed fingers | – | – | 1 | 1 | – | – | – | – | 1 |
| Ventricular septal defect | – | – | – | – | 1 | – | – | 1 | 1 |
| Mongolism | – | 1 | – | 1 | – | – | – | – | 1 |
| Stenosis rectum, bicornuate uterus matted intestines | – | – | – | – | – | 1 | – | 1 | 1 |
| Omphalocele | – | – | 1 | 1 | – | – | – | – | 1 |
| Patent foramen ovale, mental deficiency—microphthalmus | – | 1 | – | 1 | 1 | – | – | 1 | 2 |
| Multiple and unspecified | – | – | – | – | – | 2 | – | 2 | 2 |
| Total | 2 | 4 | 11 | 17 | 2 | 7 | 21 | 30 | 47 |

* For key to abbreviations, see Table II.

remaining malformations is about 1 : 1. The spectrum of the other malformations is rather wide. This is in accord with previous findings (Stevenson, 1960; Stevenson and Warnock, 1959).

It is of interest to note that both male twins in a pregnancy complicated by hydramnios developed pyloric stenosis some weeks later. This is an unusual event because twins from an hydramnios complicated pregnancy are more usually discordant in respect of an anomaly even if they are monozygotic. It is not clear whether there was hydramnios in both sacs in this case. Probably there was not and the association with pyloric stenosis is fortuitous.

One pregnancy gave rise to a stillborn male child with non-rhesus hydrops foetalis. This is not included as a malformation but it is a not uncommon association with hydramnios (Stevenson, 1960) whether as a result of purely hydrostatic considerations or not is not known. It may be noted that from the hospital notes it is clear that a high malformation rate also pertained in the cases not visited of 25 index pregnancies with hydramnios; the result was a grossly malformed child in eight cases.

Bourne and Benirschke (1960) have demonstrated a remarkable association with absence or obliteration of one umbilical artery and malformation of the foetus. Of 113 foetuses, 58 or 51 per cent were malformed. In 19 patients of 101 where "adequate information was available" the pregnancy was complicated by hydramnios and all the infants were malformed.

### *Condition of Offspring from Recurrent Hydramnios Pregnancies*

The condition of the offspring of women with recurrent hydramnios is of some interest. One woman who had hydramnios three times had three children who were not malformed. The second had two normal offspring but the child from the middle of the three hydramnios pregnancies was malformed (macerated stillbirth with omphalocele). Eight women had two so complicated pregnancies each resulting in a normal child. Two women had one malformed child and one normal and four women had malformed children from both of their hydramnios pregnancies (three having two anencephalics). Of all 34 such pregnancies in women who had hydramnios twice or more, 11 children were abnormal. It does not look as if recurring hydramnios is unduly associated with malformation.

### *Other Aspects of the Offspring*

Six of the 114 index pregnancies ended before the twenty-eighth week of pregnancy and were technically abortions. Of these six in two cases

the labour was induced. One pregnancy complicated by severe early onset hydramnios at 22 weeks resulted in non-viable but apparently non-malformed female twins and in one the foetus was recognized to be anencephalic at 27 weeks, the hydramnios again being severe and having started at 24 weeks.

In view of the high frequency of induction of labour and Caesarean section noted later, together with the high proportion of twin pregnancies and the number of anencephalics with artificially lower birth weights it does not seem justified to make comments about prematurity or birth weights.

*Condition of Offspring by Severity of Hydramnios*

Table IV shows that for recorded arbitrary severity of hydramnios grades 1 (mild), 2 (moderate), and 3 (severe), 5 in 48 (10·4 per cent), 12 in 43 (27·9 per cent), and 24 in 42 (57·1 per cent) respectively were malformed. Clearly there is a progressively increasing proportion of malformed. Table V appears to show an association between early onset of hydramnios and severity. 10/20 were grade 3 in onsets under 27 weeks whereas only 28/92 from 28 weeks to term were grade 3 (Table V). The difference is highly significant ($\chi^2=20·0$, df=1, $P<0·001$). There is perhaps some suggestion (Table VI) that severity tends to be greater in younger than in older mothers but the difference here is not statistically significant (grouping ages up to 25 and 35+ $\chi^2=7·41$, df=3 $0·10>P>0·05$).

*Subsequent Condition of Live Born "Normal" Children*

Enquiries were made about the health and progress of the children of the relevant pregnancies when the mothers were visited. The mean age of the survey children was almost exactly 5 years but the range was from 1 to 10 years. Four malformations not noted in hospital were found, the twin boys who developed pyloric stenosis at eight weeks, a child seen at nine years of age in whom a diagnosis of congenital heart disease had been made at one year and the mental defective child with microphthalmus and deafness. There were a number of children who were not making progress. Two (5 years and 4 years) were high-grade mental defectives, the condition not apparently being relatable to any specific syndrome and one seen at 4 years had occasional fits when she had any febrile illness.

It is difficult to make any deductions from so few observations.

## Association of Hydramnios With Other Complications of Pregnancy

*Diabetes*

Six mothers were diabetic including three who had hydramnios in two pregnancies. The nine pregnancies gave rise to 5 single normal live births and 4 pairs of twins. All the offspring survived and eight were normal, the exception being the child already mentioned who is mentally subnormal and with partial blindness and deafness. The association with diabetes is well known but the figures here are too small to be of value in determining malformation rates.

*Threatened Miscarriage*

In all there were only three cases of early bleeding in the series and the offspring were the male stillbirth with non-rhesus hydrops, a normal male live born child and a male stillbirth with hydrocephalus.

*Toxaemia of Pregnancy*

Toxaemia was present in 59 of the 132 hydramnios complicated pregnancies or 44·7 per cent, a much higher proportion than would be expected in a hospital series. Of 109 single pregnancies 47 were affected and of 23 twin pregnancies 12 were affected. There are always difficulties in reconciling diagnostic criteria of toxaemia by different observers but the frequency does seem higher in this series than in others recorded, e.g., Harris (1959) 29 per cent, Stevenson (1960) 25·5 per cent, Macafee (1950) 24 per cent. Data from Belfast suggested that a smaller proportion of children might be malformed where the pregnancy was complicated by both toxaemia and hydramnios than where there was only hydramnios. The present data (Table VII) do not support this suggestion.

TABLE IV

*Condition of 133 Offspring by Severity of Hydramnios*
*(114 Index Pregnancies Only)*

| Severity of Hydramnios | No. of Pregnancies | Condition of Offspring | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| | | LB (A) | | LB (D) | | SB | | Total | |
| | | Normal | Mal-formed | Normal | Mal-formed | Normal | Mal-formed | Normal | Mal-formed |
| 1. Mild .. .. | 41 | 39 | 3 | 2 | 1 | 2 | 1 | 43 | 5 |
| 2. Moderate .. | 35 | 25 | – | 1 | 1 | 5 | 11 | 31 | 12 |
| 3. Severe .. .. | 38 | 7 | – | 1 | 8 | 10 | 16 | 18 | 24 |
| Total .. .. | 114 | 71 | 3 | 4 | 10 | 17 | 28 | 92 | 41 |

For key to abbreviations, see Table II.

TABLE V

*Severity of Hydramnios by Weeks to Onset*
*(114 Index Pregnancies Only)*

| Severity of Hydramnios | Weeks to Onset of Hydramnios | | | | | | | | Total |
|---|---|---|---|---|---|---|---|---|---|
| | <20 | 20– | 24– | 28– | 32– | 36– | 40+ | Not Certain | |
| 1. Mild .. .. .. | – | 2 | 5 | 11 | 4 | 13 | 5 | 1 | 41 |
| 2. Moderate .. .. | – | 1 | 2 | 9 | 10 | 11 | 1 | 1 | 35 |
| 3. Severe .. .. .. | 1 | 5 | 4 | 10 | 13 | 5 | – | – | 38 |
| Total .. .. .. | 1 | 8 | 11 | 30 | 27 | 29 | 6 | 2 | 114 |

TABLE VI

*Severity of Hydramnios by Maternal Age*
*(114 Index Pregnancies Only)*

| Maternal Age (Years) | Severity of Hydramnios | | | Total | % Grade 3 of Total Cases |
|---|---|---|---|---|---|
| | 1 Mild | 2 Moderate | 3 Severe | | |
| 15– .. .. .. | 1 | 1 | 4 | 6 | 43·8 |
| 20– .. .. .. | 8 | 8 | 10 | 26 | |
| 25– .. .. .. | 13 | 10 | 9 | 32 | 35·7 |
| 30– .. .. .. | 6 | 7 | 11 | 24 | |
| 35– .. .. .. | 13 | 8 | 1 | 22 | 15·4 |
| 40+ .. .. .. | — | 1 | 3 | 4 | |
| Total .. .. .. | 41 | 35 | 38 | 114 | 33·3 |

TABLE VII

*Condition of Offspring from 132 Hydramnios Pregnancies Where Toxaemia Was or Was Not Also Present (Single Births Only)*

| Toxaemia | Condition of Offspring | | | | | | Total | | |
|---|---|---|---|---|---|---|---|---|---|
| | *LB (A) | | LB (D) | | SB | | | | |
| | Normal | Mal-formed | Normal | Mal-formed | Normal | Mal-formed | Normal | Mal-formed | Total |
| Present .. | 22 | – | – | 5 | 5 | 15 | 27 | 20 | 47 |
| Absent .. .. | 35 | 1 | 1 | 6 | 3 | 16 | 39 | 23 | 62 |
| Total .. | 57 | 1 | 1 | 11 | 8 | 31 | 66 | 43 | 109 |

* For key to abbreviations, see Table II.

Indeed there is a higher proportion of malformations when the pregnancy is also complicated by toxaemia although the difference is not technically significant.

*Hyperemesis*

Of the 114 index hydramnios pregnancies, 13 (11·4 per cent) had been recorded as having had hyperemesis during the earlier period of the pregnancy. This may be compared with 103 (0·6 per cent) cases in 15,967 pregnancies in the hospitals over the period.

*Ante-partum Haemorrhage*

Ante-partum haemorrhage occurred in 12 cases—in three with previously recorded toxaemia. There were seven stillborn anencephalics in the offspring. There was nothing to suggest that any were associated with placenta praevia and most were probably of mechanical origin following rupture of the membranes, although only in six cases was the hydramnios classed as severe.

*Post-partum Haemorrhage*

Post-partum haemorrhage occurred eight times in 132 deliveries (6·1 per cent) but was in no case severe. This compares with 1,093 cases of post-partum haemorrhage as reported in 15,967 births in the hospital series or 6·8 per cent.

*Prolapsed Cord*

In the confinements of the 114 index pregnancies prolapsed cord was noted only on two occasions (Seligman, 1960). One resulted in a live born girl who is backward and has fits so presumably the complication may have occasioned anoxia. The other resulted in a male intra-partum stillbirth with ventricular septal defect, pulmonary stenosis and webbed fingers.

This does not suggest any strong association with hydramnios—a finding in accord with those of Seligman (1960).

*Induction of Labour*

Lower segment Caesarean section was the mode of delivery in seven of the 114 index pregnancies. In the remaining 107 pregnancies labour was induced by rupture of the membranes in 62 cases or 57·9 per cent. This high induction rate determines that data for duration of pregnancy and birth weights of the children are impossible to interpret or to correlate in any useful way with severity of hydramnios. Two of the inductions were prior to the 28th week and resulted in one normal stillbirth and one anencephalic. In the remaining 60 cases the child was malformed in 21 cases and apparently normal in 39 cases.

The commonest reasons for induction were radiographic demonstration of an abnormal foetus, concomitant toxaemia and severity of subjective symptoms in the patient.

*Presentations at Vaginal Delivery*

In the 88 index single births delivered *per vaginam*, the presentation was as vertex in 71 (80·7 per cent), shoulder 1, breech 12 (13·6 per cent), and face 4 (4·5 per cent).

There is probably therefore some increase in abnormal presentation frequencies.

*Mode of Delivery*

Lower uterine segment Caesarean section was used in eight of the 132 and in seven of the 114 index pregnancies. The indications seemed to have been malpresentations in the elderly primigravida and infertility. It is interesting to note that there was no foetal wastage or malformation, all sections resulting in normal children who have survived. Of the remaining 107, 19 were twin pregnancies. Of the 88 singletons delivered *per vaginam*, 27 (30·7 per cent) were forceps assisted deliveries.

*Outcomes of Pregnancies not Complicated by Hydramnios*

These are summarized in Table VIII.

By the time that they were visited the mothers were on average five years older than when they had the index hydramnios pregnancies. Of the 255 pregnancies in these mothers which were not complicated by hydramnios 34 or 13·3 per cent ended in abortion. This is not an unduly high figure for spontaneous abortion (Stevenson *et al.*, 1959).

In the remaining 221 pregnancies terminating after 28 weeks there were three pairs of twins (all alive and normal, two male and one male/female pair) so in all there were 224 offspring.

There were two males with spina bifida who survived, two siblings had Arnold-Chiari malformation (their remaining sibling from an hydramnios pregnancy was a female stillborn anencephalic) and a female with horse-shoe kidney who survived (she is a sibling of the male twins with pyloric stenosis from an hydramnios pregnancy).

These five malformed in 224 offspring do not suggest any marked rise in the malformation rate in these pregnancies.

## Discussion

Similar aspects of the problem of hydramnios have recently been discussed rather fully (Stevenson, 1960) and need not be elaborated

Table VIII

*Condition of 258 Offsprings of 255 Pregnancies Not Complicated by Hydramnios*

| Outcome of Pregnancies | | Males | Females | Sex Not Known | Total |
|---|---|---|---|---|---|
| Alive, not malformed | Single .. .. .. | 112 | 93 | 1 | 206 |
| Alive, not malformed | Twin pairs .. .. | 5 | 1 | – | 6 |
| Alive, malformed | Single .. .. .. | 2 | 1 | – | 3 |
| Died, not malformed | Single .. .. .. | 2 | – | – | 2 |
| Died, malformed | Single .. .. .. | 2 | – | – | 2 |
| Stillborn, not malformed | Single .. .. .. | 1 | 3 | 1 | 5 |
| Stillborn, malformed | Single .. .. .. | – | – | – | – |
| Abortions .. .. .. .. .. .. .. | | – | – | 34 | 34 |
| Total .. .. .. .. .. .. .. | | 124 | 98 | 36 | 258 |

here. There is nothing very surprising about the data presented but there are a number of deductions which seem to be worth underlining.

(1) The most obvious is the very high malformation rate in the offspring, the commonest being anencephaly but a wide spectrum of other malformations are associated. Taking the Oxford and Belfast data together the range is remarkably wide and seems impossible to rationalize with any theory of lack of swallowing of liquor by the foetus being a necessary condition for hydramnios.

(2) There is no very marked association of hydramnios with maternal age and parity.

(3) Hydramnios tends to recur in subsequent pregnancies and the risk of recurrence after the first hydramnios complicated pregnancy seems to be about 1 in 4. As the malformation rate is about 1 in 3 perhaps 1 in 12 of infants born to a mother subsequent to a pregnancy complicated by hydramnios may be expected to be malformed. This is perhaps a useful empirical risk to bear in mind in view of questions so often asked about the future. These and the Belfast data suggest, however, that if the first hydramnios pregnancy resulted in a malformed child then the risk of a subsequent malformed child is rather higher.

(4) Hyperemesis tends to be a precursor of hydramnios more frequently than would be expected by chance and as is well known diabetic mothers tend to have hydramnios in pregnancy. Both these associations may explain in turn the small associations between hyperemesis and between diabetes and malformations in offspring.

(5) Work of this kind throws no light on the aetiology of hydramnios or on whether the primary stimulus to hydramnios lies in the maternal or foetal genotype. As, however, hydramnios is so much more strongly associated with malformation than any other complication of pregnancy there does seem to be urgent need for clinical and laboratory research into the mechanisms involved. It should be noted in passing that no known single gene determined abnormality is associated but that at least two chromosomal aberrations are associated, namely, mongolism and the syndrome associated with trisomy of the 17th chromosome described by Edwards *et al.* (1960) and since then by other observers. It is important to record whether hydramnios occurs in pregnancies leading to other types of offspring with chromosomal anomalies.

## Summary

An account is given of the other characteristics of the pregnancies and of the condition of the offspring of 114 mothers who were identified by having at least one pregnancy complicated by hydramnios. In so far as is possible from the limited data the closeness of these associations is examined.

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# INFERTILITY OF EMOTIONAL ORIGIN

BY

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## INTRODUCTION

IN the past, perhaps through ancient Biblical teaching and the conceit of men, infertility has been regarded as primarily a female affliction and treated, often reluctantly, by the gynaecologist alone. Increasing interest in this subject during the last two decades has brought to the study of infertility a more scientific assessment of the roles of both partners in a marriage. This, however, has introduced new hazards because modern medicine has developed primarily as a study of organ dysfunction and there has been a tendency to overlook the fact that it may be the whole patient that requires treatment. Yet as Menninger said many years ago, "her illness represents a psychic conflict sailing under a gynaecological flag" (Menninger, 1943). An investigation of the problem of infertility which consists only of a list of lesions found and which does not explain why these lesions occur, or why, when the faulty parts are corrected, the infertility is still maintained, is not an adequate approach to the subject.

It is a common experience that infertility has been "cured" after years of sterility following very varied events which could apparently have had no organic effect on the patient. For example, conception has followed the making of an appointment even before the consultation took place, or after arrangements for a semen analysis, even before the results were known. "Cures" have also occurred after a simple vaginal examination, after general reassurance, and after the patient has applied for the adoption of a child. Sharman (1952) noted a large series of cases in which conception occurred after the passing of a sound into the uterus or after an endometrial biopsy. The only common factor in all these antecedent events is that of the relief of tension.

The ancients anticipated us in their treatment of the emotional causes of infertility. At least they were aware of the successes which followed rituals, incantations and rites, even if they did not know that they were treating tension and depressive states. It may be therefore that those of us who are surgically minded have been deceiving ourselves when we thought that it was our therapeutic techniques which cured all our patients; we may only in fact be using "ourselves, as doctors, as the therapeutic instrument" (Balint, 1955).

Evidence from many sources seems on the whole convincing that there can be a physiological stress response to a human "problem–situation" and the chain of events "situation→stress→symptoms" may form a clearly recurring pattern, and that, no matter what type of treatment is instituted, the relationship with the therapist himself is one of the most important factors.

## EVIDENCE FROM CASE HISTORIES

Study of case histories will often show abnormal attitudes to parenthood, and this is confirmed by the frequent failure of artificial insemination, either by donor or from husband. De Watteville (1957) noticed that women, who menstruated regularly when first seen, failed to ovulate when artificial insemination was planned. Pregnancy, childhood and parenthood are threatening states, at both conscious and unconscious levels in some women, and this may result in either designed avoidance of conception or inactive acceptance of the infertility. Many of

us now realize that the intensity of the complaint about infertility indicates that beyond conscious knowledge and control, there exists a drive to remain sterile.

A woman, aged 34, had been sterile for ten years, despite numerous curettages and other investigations. She was referred to me by an orthopaedic surgeon who could find no physical cause to account for the severe pain she had in her hip and suspected some kind of sexual maladjustment. Study of her story revealed that she was the owner of a dancing school and was in considerable conflict because the arrival of a child would mean giving up the school and reducing her standard of living. One half-hour's discussion sufficed to give her insight into her unconscious rejection of pregnancy, and I made her face the decision consciously whether or not to close the school. She decided to do so, and conceived the next month without any other treatment.

A wife, aged 21, shared her home with a medical student brother and always consulted him about each failure to achieve successful coitus. The dependence of this woman on her brother had to be overcome and a mature relationship with her husband established before full orgasm was achieved, followed quickly by conception.

A woman, aged 30, unconsciously rejected her husband. She had married him on the rebound when her first choice (with whom she had had successful coitus) failed to marry her. This woman never achieved satisfactory orgasm with the second partner, who was lacking in finesse, and conception only occurred when she had put her name down for adoption.

A woman, aged 29, had been married to a drunkard who was unfaithful while she was in hospital bearing his first child. She divorced him and remarried happily, but could not produce a second child, although there was no abnormality found when she was investigated at another hospital. She confessed on questioning that she was never able to achieve orgasm because "she was afraid to let herself go". The basis of this was fear that the second husband might also be unfaithful while she was in hospital with a pregnancy.

A woman, aged 26, achieved occasional unsatisfactory orgasm with her extrovert husband. She herself was very introspective, suffered from colitis and could not stand up for herself against a mother-in-law who interfered in her affairs. Each unsuccessful argument was followed by an attack of diarrhoea. This woman was given insight into her problems and helped to stand up for herself. Conception occurred without any specific treatment for her internal organs.

I have analyzed the histories of 268 consecutive childless marriages to see what proportion had an important emotional stress element in the backgrounds of either partner. In these 268 cases there were 67 considered to be provoked by stress totalling 25 per cent. In these 67 cases there were 32 pregnancies equivalent to 48 per cent whereas, in the remaining 201 cases in which emotion was not considered to play an important part, there were 64 pregnancies equivalent to 32 per cent. These pregnancy rates show close agreement with the figures of Stone and Ward (1956) and Peberdy (1958) and justify the conclusion that a quarter of all women seen at infertility clinics will have stress as the main cause of their disorder.

TABLE I

| | | | % |
|---|---|---|---|
| Emotional immaturity in one or both partners | 29 | = | 43 |
| Impotence | 15 | = | 22·5 |
| Ignorance of sex technique | 14 | = | 21 |
| Pregnant before investigation | 6 | = | 9 |
| Vaginismus and frigidity | 5 | = | 7·5 |

By far the largest group of cases is that of emotional immaturity which quite often affects both partners. It is noteworthy how in the emotional sphere as well as the physical one, the phenomenon of assortative mating (Slater and Woodside, 1951) also occurs, and immature personalities do seem to attract each other. Many of these women subconsciously reject parenthood. In some, rejection of parenthood and subconscious rejection of husband go together. In other cases it is the husband who rejects parenthood and this may adversely affect his wife emotionally.

A woman of 28 unwillingly married a man because he was her last chance but did not correspond with the ideal for whom she was searching. She admitted that coitus was unsatisfactory and that during the act she was in a state of fantasy in which she dreamt that it was not her husband who was having intercourse with her but rather the dream ideal figure which she had always imagined would be her husband. It is not surprising that with the rejection of reality which goes with such a state of mind, there of course went a rejection of the realities that parenthood and maternity must entail.

Confusion has arisen in assessing the effects of treatment in infertility in the past, because the doctor has neglected to take into account the patient/doctor relationship and the therapeutic effect of his own personality. A woman may conceive not because of any particular physical treatment but because she is emotionally ready to deal with conflicts about conception. The question we should ask ourselves is: does she really want to conceive, and is she mature enough for pregnancy? In the treatment of infertility the idea that the doctor's attitude really matters requires a new approach and indeed poses social questions of fitness for parenthood hitherto not considered.

A woman, aged 27, came from a broken home where her own mother's illness had necessitated a leucotomy. She was afraid that she might not be able to stand the strain of rearing a child and so repeating the pattern of her own family. A pregnancy was in fact obtained. Six months later she had already visited her doctor asking for help as she had an impulse to kill her child!

A teacher, aged 36, was married to another teacher and she was over-anxious about her ability to conceive. She twice achieved conception but aborted. She then decided to adopt and the day before a baby should have arrived, she found she was pregnant. At delivery there was severe dystocia necessitating Caesarean section for inertia (a not uncommon complication in this type of case) and nine months later she committed suicide.

Sterility can thus be a defence of the disturbed personality against the experience of pregnancy and motherhood. The equality of the sexes, which our present-day society fosters, tends to make a woman less submissive, and her ego appears to be stronger; she has aspirations which may indeed be in conflict with the function of reproduction. In previous generations, childbearing and the rearing of children were frequent events absorbed by the daughter of the household as she grew up and as part of her natural background. In our generation, such a daughter may have one or at the most two pregnancies occurring in her mother on which to base her impressions. Hence, conception may be unwanted and may produce conflicts in the woman—especially if she is trained for a profession or a skilled trade. The popular image today of maternity is less that of a simple and natural process to which the woman should look forward, but instead an alarming experience arousing fear and trepidation. Often pressures from husband, relatives and friends urge the married woman to contemplate childbearing as desirable, when the very idea of it may be frightening. A useful question is: why does a sterile woman want to have a child? Some remarkable answers have been forthcoming: to satisfy the husband's demands; to be like other women; to have something of her own; to have somebody to love her; to show her mother how a child *should* be brought up; to patch up a shaky marriage; to gain the affection which her own husband does not give her. The uniform tension in the background of these women enables one to make a positive diagnosis not by exclusion but on factual evidence. Their stories so often reveal the failure of these women to adapt themselves to the demands of a mature interpersonal relationship, not only in the sexual sphere, but in every aspect of life. Indeed they respond to the threat of pregnancy by a chronic state of anxiety and tension.

## The Nature of Stress

The term "stress" is here taken to mean "the internal or resisting force brought into being in the human organism by interaction with the environment" (Wolff, 1952). Benedek (1952) has shown that "any symptom is an attempt to safeguard the organo-psychic equilibrium". We may put this more simply by saying that these

patients need their symptoms and the removal of psychosomatic symptoms without treatment of the underlying conditions has sometimes produced a breakdown in the patient (see page 810). Kroger and Freed (1950) have defined infertility of emotional origin "as those cases where there is no demonstrable endocrine dysfunction or organic disease" but this seems to be a diagnosis by exclusion and hence incomplete. With J. Sandler (1958), we may ask "what is the step between the psychological factors in symptom-formation on the one hand and the somatic language on the other?" Wolff (1952) has shown that an emotional stimulus causes autonomic effects on specific parts of the body and indeed speaks of "stomach reactors", "chest reactors", "nose reactors".

We are all familiar with the man who develops asthma or a duodenal ulcer under emotional stress but we should enquire why the asthmatic always get asthma and not an ulcer or a sinusitis. Gellhorn (1957) has shown that segmental autonomic reflexes increase the reactivity of a certain organ specifically so that it will react to hypothalamic discharges more than do other parts of the body.

This work is confirmed by the experimental work of Bruce (1959) who, with mice, found that under control conditions the emotional stress of placing a strange male in proximity, but without physical contact, with a recently mated female would block the pregnancy in that female by exteroceptive means and she concludes that both pituitary and hypothalamic influences are probably implicated.

In view of the work of Gellhorn we must expect emotion to have a profound effect on tubal function and this has indeed been the case in my experience. The following two cases illustrate this point very clearly. Insufflation of a woman aged 24 who was very tense and nervous, showed apparent occlusion with no peristalsis at 200 mm. of mercury. She was so nervous that I tried to distract her attention by making a joke and she immediately burst into laughter. As she laughed the needle dropped to 40 mm. pressure, gas passed with peristalsis and she conceived that same month.

A farmer's wife, aged 28, sterile for 2 years had slight but definite vaginismus. All tests were normal except for severe tubal spasm on insufflation and salpingography. She was treated with Merbentyl and phenobarbitone and I noted that the gas then passed easily through the tubes, with peristalsis, whilst I was holding her in conversation. Immediately I told her that the gas was passing she developed intense spasm, the pressure rose to 200 mm. and no further gas passed. She had many times postponed her appointment because of alleged difficulties on the farm and I felt this to be evidence that this woman unconsciously rejected pregnancy because of the trouble she foresaw in running a farm and having a baby.

The recurring pattern "situation→stress→symptom" is so clearly manifest in many of these cases that it is not difficult for those who are aware of the concept of stress to recognize them as primarily problems of personality rather than physical disorders of the genital organs. I propose, therefore, to examine some of the causes of infertility found in married couples and try to show how what has in the past been regarded as a condition of organic causation may, in fact, be the somatic response to a stress-situation involving the whole personality.

## Faults in the Coital Act

In certain cases of organic defect, such as hypospadias, there will be mechanical failure to deposit the semen in the vagina at all. Such cases require no further comment within the context of this paper.

A number of men, however, have been referred to me who have had tuberculous orchitis and they or their advisers have blamed their infertile marriage on this disease. In certain cases, however, one with an unhealed fistula and others with a healed and rather atrophic testis on one side, the semen quality was normal and the men were in fact suffering from premature ejaculation or intermittent impotence mainly due to the anxiety neurosis which they had developed consequent on their knowledge that the testes had been damaged by the disease. All these cases responded to reassurance and no physical treatment was indicated or given. It is interesting to note that had these men been given testosterone, for example, plus the reassurance

that all would be well, the cure might have been attributed to the hormone rather than the reassurance which accompanied it.

In another case a man had had excision of the rectum for carcinoma which was followed by impotence. The surgeon concerned thought that the nerve supply might have been damaged during the extensive operation required and referred him to me for a second opinion. After considerable investigation, I found that this man was impotent not from physiological reasons as a result of the operation but from psychological reasons, since he had a mistress and had not, in fact, slept with his wife for many years as she had always refused coitus.

Premature ejaculation is a condition frequently met with in the early stages of a marriage, but it may persist and invariably the mechanism is emotional in origin. Usually the partners are aware of the existence of the condition, but not always, and in a certain number of cases ejaculation takes place before penetration has occurred, without the couple realizing that this has happened. More particularly there is great ignorance of the technique of coitus both physiological and psychological. Many workers, Stallworthy (1948), Green-Armytage (1948), Sharman (1952), as well as myself found that an average of 5 per cent of all women attending an infertility clinic are virgins, intercourse taking place between the thighs and neither party being aware of the absence of penetration. In an even larger group, penetration is inadequate not from causes such as vaginismus or frigidity but simply due to failure to adopt the correct posture, and a general lack of finesse on the part of the husband. That the wife has an important positive part to play in the act of coitus is unknown to many of these couples and the failure to achieve either penetration or orgasm leaves such women with congested pelvic organs, stimulated but not satisfied, and often in a state of emotional frustration as well as physical discomfort after the act. The coital history and adequacy of orgasm are, therefore, extremely important factors in the assessment of these cases. This assessment is made more difficult because, in a woman, sexual frustration is not something which she will be aware of herself unless she has had some kind of sex instruction. Such women are often unable to correlate their general irritability, frustration and nervous tension with their failure to achieve sexual satisfaction, yet the effects can be profound and far-reaching and infertility may only be one among many of the disturbances of the whole personality which can occur in such cases.

Such gross physical disturbances as leucorrhoea, menorrhagia and backache with dyspareunia may occur—and these, of course, will not respond to medicinal measures so long as the cause remains. Nevertheless, there are many women with these symptoms who have been treated for years with a variety of physical treatments without cure, because the vision of their doctors is limited to the pelvis, and the personality of the patient and her reaction to the problems of her environment are completely neglected. Morris and O'Neill (1958) have shown that in a large group of women visiting an ordinary gynaecological clinic and investigated simultaneously by a gynaecologist and a psychiatrist, a very high proportion of the symptoms could be attributed to emotional disturbances and were, in fact, cleared up without any physical treatment whatsoever. In contrast, Davis (1958) does not believe that such problems exist and "finds it difficult to believe that emotional stress alone can actually initiate gross symptoms, particularly pain". That such attitudes are still very prevalent is, in my view, responsible for much mis-diagnosis and inadequate treatment.

### Disturbances of Menstrual Cycle

Whenever the chain of communication is interrupted between cerebral cortex or hypothalamus and the genital organs, ovulation will be disturbed and amenorrhoea will occur. Some of these phenomena are well known as, for example, any novel situation affecting the young, such as entry to college or becoming nurses or in periods of domestic crisis or after severe fright. Fifty per cent of women in prison camps during the war had amenorrhoea and 10 per cent of women exposed to rape have amenorrhoea also.

Amenorrhoea can also be the result of a

guilty conscience in a girl who has exposed herself to the risk of pregnancy. The opposite effect of functional bleeding is well known (Blaikley, 1949). Stieve (1952) records the onset of bleeding in women about to be executed and Heiman (1956) records, as do many others, functional bleeding within one hour of psychological trauma. Stauder and Tscherne (1953) described 7 women who remained sterile after having lost a child during delivery or by accident. All findings were normal except the basal temperature charts which showed anovulatory cycles. The psychic trauma had impaired gonadotrophin production but pregnancy followed psychotherapy in all 7 cases. It is known (Heckel and Tobin, 1956) that there are arteriovenous shunts in the endometrium of the human uterus of which the control is not fully understood. In this connexion the work of Loeser (1943) is important. He described the case of 4 women exposed to bombing during the war years; this exposure was followed by a sudden onset of amenorrhoea. The endometrial biopsies of all 4 were sent to E. Novak in America in order to find the day of the cycle at which the endometrial development had been arrested. Novak "dated" each one and his conclusion was found to correspond with the very day of the menstrual cycle on which each woman had been exposed to the shock. This seems convincing evidence that emotional upsets can produce an immediate effect on the menstrual cycle. I have noted repeatedly that an immature woman often has hypogonadal genitalia and suffers from intermittent amenorrhoea due to her failure to ovulate. These women often have low hormone levels and indeed in some the administration of oestrogen by mouth or directly into the uterus by injection (Field-Richards, 1955) has been shown to promote uterine growth. I have also noted that the same type of woman, who has undergone adequate psychological investigation, gained insight into her problems and achieved a satisfactory adjustment both sexually and emotionally with her husband, soon begins to obtain adequate coitus with orgasm and subsequently in many cases the uterus is found to have grown without any other treatment. This is a further example of somatic response to emotional change.

If the cervical mucus is absent, deficient or hostile, penetration by spermatozoa will not take place and the patient will be infertile. I have shown (Sandler, 1952, 1953) that a high proportion of infertile patients have bacterial infection of the cervix which becomes non-receptive to all types of spermatozoa whereas a similar series of healthy women who came for advice about contraception were found to have no pathogens by mucus culture. I took the view then that the presence of bacteria alone was the cause of the negative post-coital test and of any alterations in the cervical mucus. In one case, however, that of a woman aged 26, I found the post-coital test negative, and the mucus scanty and dry, and I recovered *Escherichia coli* from culture of the cervical mucus. It seemed at that time clear evidence that this might be the cause of her infertility. Owing to a change of address, no treatment was instituted and she did not attend again until three years later, still sterile. Her cervical mucus was now clear, the post-coital test satisfactory although still no treatment had been undertaken. She admitted upon enquiry that whereas three years previously there had been serious maladjustments both in the sexual and in the family spheres, these had now been resolved and she was very much happier. It would seem, therefore, that the organic changes which I had originally observed were in fact the result of somatic defence mechanisms. Since then I have seen many women with a dry cervix, scanty sticky mucus and other evidence of hypogonadism, the result of emotional tension. It is not sufficient merely to record an observed organic lesion as being the sole "cause" of the patient's troubles. To look at the cervix and forget the patient is to be in the same position as the man who looks at the mouth of a terrified woman, notes that it is excessively dry, and then proceeds to prescribe a mouthwash! The irrationality of such "treatment" is self-evident when the symptom is a dry mouth; it is not perhaps quite so obvious when it is a dry cervix. Yet how often is the patient asked if she is happily married, or whether she has an orgasm? In my experience, a high proportion of patients do not have orgasm, and consequently receive continuous sexual stimulation

without satisfaction; this leads in turn to chronic pelvic congestion, which is one of the commonest causes of the non-receptivity of cervical mucus.

Dunbar's (1952) statement that "pregnancy cannot be taken as a proof of cure of infertility" has some significance. We must beware of forcing these patients by therapeutic means into a role for which they are unprepared. The task of establishing a connexion between states of mind and bodily events is ever present in "psychosomatic medicine". It is one to which insufficient attention has been paid by many of those who have to deal with infertility. I hope that this paper will serve to draw attention to the importance of a biological approach to this disorder.

## Summary

A definition of stress is given and the application of this concept in infertility is outlined. The relationship between stress and infertility is described. The proportion of cases of infertility of emotional origin is given in an analysis of 268 consecutive marriages seen in an Infertility Clinic. About one-quarter of all cases seen have stress which can maintain the infertility even when the genital lesions have been successfully treated. A plea is made for a new approach. Infertility may be one of the signs of emotional disturbance. Therapy is directed to the relief of tension. An analysis of the incidence of such cases and a table of the types of emotional stress found are given.

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# CERVICAL CARCINOMA IN AN IDENTICAL TWIN

BY

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IF carcinoma of the cervix is found in one of a pair of monozygotic twins what is the chance that the other will also develop cervical carcinoma? The literature on this question does not appear to be extensive; the problem has been studied by von Verschuer of Munster (1956) and Neilsen and Clemmesen (1957) of the Danish Cancer Registry.

Briefly, the method is that when one twin, monozygotic or dizygotic, is registered as a cancer patient, the other twin is examined and followed up if available. von Verschuer, in twenty-six sets of monozygotic twins, of both sexes, found concordance of type and site of cancer in three sets, all gastric carcinoma. In a collected series of 120 sets of monozygotic twins only 16 suffered from uterine cancer, and in only one of these sets was concordance found. He also found concordance in 4 of the 21 sets of binovular twins suffering from uterine cancer.

Neilsen and Clemmesen, in a total of 45 sets of monozygotic female twins, found only one case of concordance in type and site, carcinoma of the right breast in both twins. They also found one pair of dizygotic twins who both developed carcinoma of the cervix, one at 31 years of age and the second at age of 36 years. They state that the apparent concordance in cervical cancer may be due to exogenic factors, or to the similar sex habits of identical twins.

Thus it is seen that the chance of the second twin developing cervical carcinoma is small. Yet there is the most interesting case reported by Ikle (1956) of the monozygotic twins, Nellie and Ursula, who reported with bleeding within six months of each other at 44 years of age. Both had cervical carcinoma Stage 2, both growths were epitheliomata. Nellie had a small flat ulcer with paracervical infiltration. In Ursula the whole of the portio was affected; the disease extended into the endocervix and paracervical infiltration was present. There was a striking difference in the life history of the twins. Nellie had married at twenty-nine years of age and had borne four children. Ursula was unmarried and had an unruptured hymen at the time of her first examination.

In March, 1960, a fair-haired patient attended my Gynaecological Clinic. I recognized her as an old patient who had been under my care on and off for several years. I asked her what had brought her back this time. To my astonishment she told me that I had never seen her before and that my previous patient was her sister. I realized that they were identical twins, this was Mary, my previous patient was Maureen.

*Mary* complained of a discharge of six to seven months' duration which had recently become offensive, and of irregular bleeding for approximately the same period. For possibly as long as twelve months post-coital bleeding had occurred occasionally and she had some dyspareunia. On examination she was found to have a carcinoma of the cervix, clinically Stage 1. This diagnosis was confirmed by examination under anaesthesia and biopsy. The pathological report stated it to be a squamous epithelioma Grade 3. A Wertheim hysterectomy and pelvic lymphadenectomy was carried out on 25th March. The specimen showed that the growth was more extensive than it had appeared to be clinically; one of the glands from the left pelvic wall was invaded. The sections showed an anaplastic squamous-celled carcinoma.

*Maureen.* It was decided that Maureen should be investigated. She was seen in the clinic on

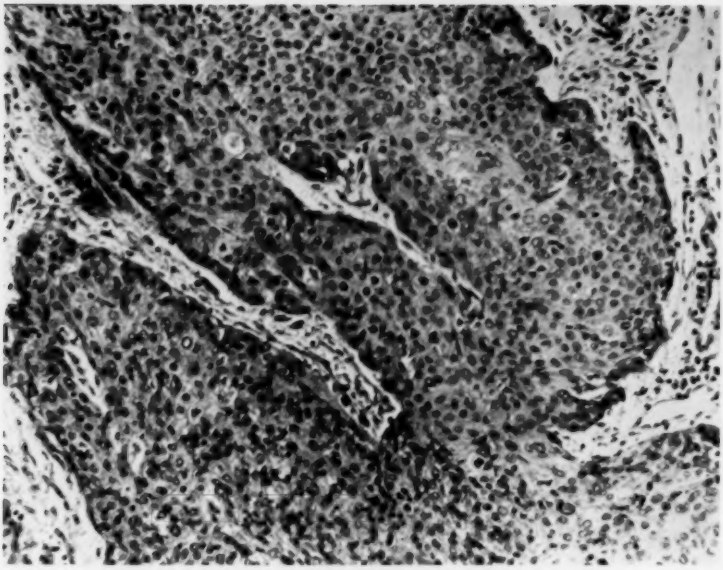

FIG. 1

Mary H. Biopsy of cervix. Carcinoma of cervix, Broder's Grade 3. ×100.

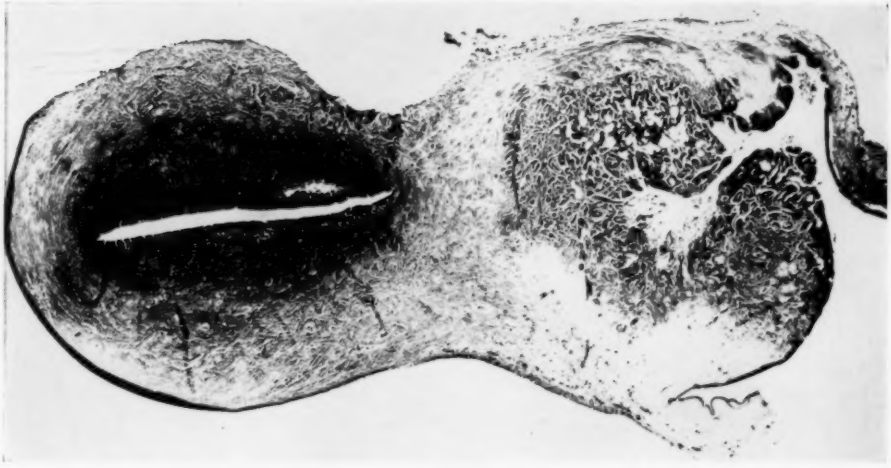

FIG. 2

Mary H. Giant section of uterus. Wertheim specimen showing the extent of the carcinoma. ×1½.

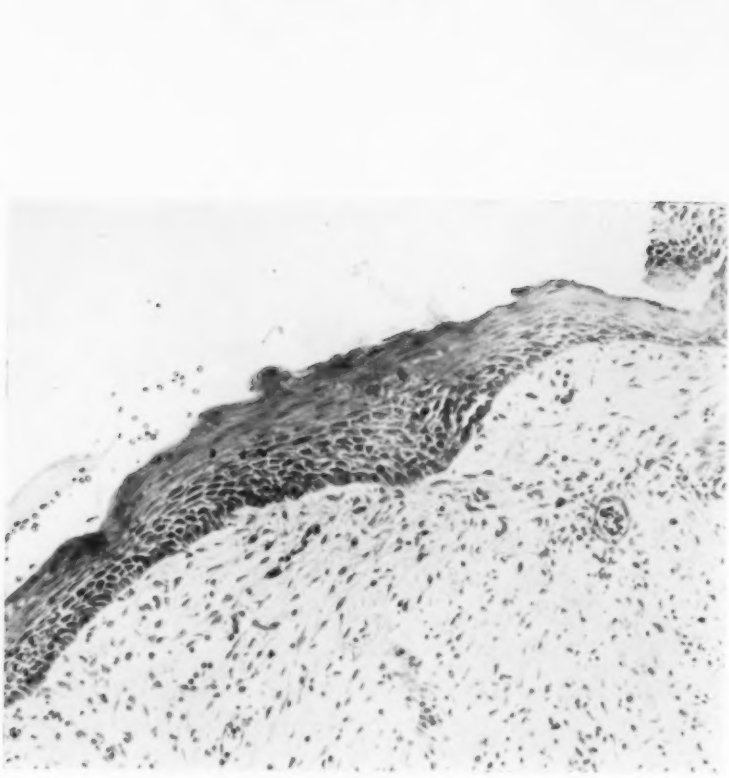

FIG. 3

Maureen J. Biopsy of cervix showing intra-epithelial carcinoma. ×100.

14th April, 1960 when a small cervical erosion was present but no other abnormality found. Owing to domestic difficulties she was unable to come into hospital immediately. On 29th June she was examined under anaesthesia. The cervix now looked perfectly healthy, there were no abnormal findings. A ring biopsy was taken; the report was as follows: "Sections of the cervical biopsy show hypertrophy and oedema of the superficial layer; chronic inflammatory cell infiltration. In one or two areas the superficial epithelium shows early microscopical malignant change. Carcinoma *in situ* early." After a careful review of the section with Dr. A. A. Miller, the condition was discussed with Maureen who readily consented to an operation. On 6th July, 1960, a total hysterectomy, conserving her left ovary and tube, was carried out. The pathological report on the cervix was as follows: "In section of the pars vaginalis and the endocervical mucosa, there is clear evidence of intra-epidermal carcinoma or carcinoma *in situ*. A few of these areas appear active but there is no invasion of the basement membranes or underlying stroma."

Unlike the Swiss twins, Mary and Maureen's previous history had been very similar. They were born in 1927 the result of their mother's only pregnancy. Both parents are alive; the mother is a diabetic. (Table I.)

This case is presented as an answer to the question what should be done when carcinoma is found in one of a pair of identical twins. It suggests that investigation of the second twin is worthwhile in spite of the rarity of concordance. The surprising fact is not that concordance sometimes occurs, but that it does not always occur, the twins having started life as one individual. If the reason for this was known it might be a pointer to the causation of cancer.

Finally, I would like to express my thanks to Dr. A. A. Miller, Pathologist, Mr. Ramsden, Senior Technician of the Pathological Department, Preston Royal Infirmary, for the time and great trouble they have taken in the production of the slides and pictures for this case.

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TABLE I

| *Mary* (33) | *Maureen* (33) |
|---|---|
| Married | Married |
| Menarche, 17 years | Menarche, 17 years |
| Periods, 3–4/28 | Periods, 3–6/28 |
| 1945 Full term normal ♀ | 1948 Full term normal ♀ |
| No other pregnancy | 1949 Premature, neonatal death |
| 1958 Appendicectomy | 1950 Abortion |
| *Blood:* O Rh. positive | 1953 Abortion |
| Wassermann reaction, negative | 1956 Full term normal ♀ |
| | 1959 Right salpingo-oöphorectomy and appendicectomy |
| | 1959 Dilatation and curettage for menorrhagia |
| | *Blood:* O Rh. positive |
| | Wassermann reaction, negative |

# INTERNAL CERVICAL OS DURING THE SECOND HALF OF PREGNANCY

BY

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## INTRODUCTION

WHILE performing vaginal examinations on women in the latter half of their pregnancy, the authors had often noticed that the internal os of the cervix allowed the passage of a finger. This observation led to a desire to study the condition of the internal cervical os during the second half of pregnancy. The present study was, hence, undertaken. When during the course of the study it was revealed that in many cases the internal os admitted an examining finger, it was considered imperative to find out whether these cervices carried any functional significance.

## MATERIAL AND METHODS

Six hundred and fifty-five patients, attending the prenatal clinic of the Nowrosjee Wadia Maternity Hospital, Bombay, were chosen for this study without any selection other than that cases of habitual abortion were excluded. The period of gestation in all these patients was 21 weeks or more. No studies were done after 36 weeks of gestation.

The internal cervical os was studied in all these cases by one or the other of the authors personally by making a vaginal examination with due precaution to ensure asepsis. If an examining finger could be introduced through the internal os, the latter was labelled as being "open" for the purposes of this study. The remaining cases, including the ones in which the external cervical os was closed were labelled as having "closed" internal os.

All the patients were called for repeated examinations at intervals of 2 weeks. Unfortunately, only a small proportion of them presented for such repeated studies.

However, the patients were traced when they attended the hospital for delivery and the outcome of the pregnancy was recorded and correlated with the character of the internal cervical os during pregnancy.

Statistical calculations were done as described by Mainland *et al.* (1956).

## RESULTS

In all, 866 examinations were done on 655 patients. Three hundred out of these 866 examinations revealed an open internal os while the remaining 566 revealed a closed internal os (Table I). This means that when random vaginal examinations are done between the 21st and 36th weeks of pregnancy, in 34·6 per cent of instances the internal os is found open. Figure 1 correlates the character of the internal os with the duration of the pregnancy at the time of the examination and it can be readily seen that, as the duration of pregnancy

TABLE I

*Internal Cervical Os at 866 Vaginal Examinations During the Second Half of Pregnancy*

| Parity | I | | II | | III | | IV | | V and Above | | All | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Period of Gestation in Weeks | Open Os | Closed Os | Open Os | Closed Os | Open Os | Closed Os | Open Os | Closed Os | Open Os | Closed Os | Open Os | Closed Os |
| 21–22 .. .. | 1 | 7 | – | 11 | – | 11 | – | 8 | – | 7 | 1 | 44 |
| 23–24 .. .. | 4 | 11 | 4 | 22 | 1 | 20 | 1 | 12 | 1 | 16 | 11 | 81 |
| 25–26 .. .. | 2 | 35 | 3 | 21 | 1 | 11 | 3 | 14 | 6 | 27 | 15 | 108 |
| 27–28 .. .. | 8 | 23 | 19 | 33 | 12 | 26 | 6 | 30 | 10 | 53 | 55 | 165 |
| 29–30 .. .. | 7 | 16 | 16 | 12 | 11 | 14 | 6 | 23 | 19 | 31 | 59 | 96 |
| 31–32 .. .. | 4 | 9 | 21 | 7 | 9 | 7 | 7 | 7 | 17 | 9 | 58 | 39 |
| 33–34 .. .. | 7 | 5 | 5 | 2 | 9 | 1 | 12 | 2 | 19 | 8 | 52 | 18 |
| 35–36 .. .. | 8 | 4 | 11 | 2 | 11 | 4 | 8 | 1 | 11 | 4 | 49 | 15 |
| 21–36 .. .. | 41 | 110 | 79 | 110 | 54 | 94 | 43 | 97 | 83 | 155 | 300 | 566 |

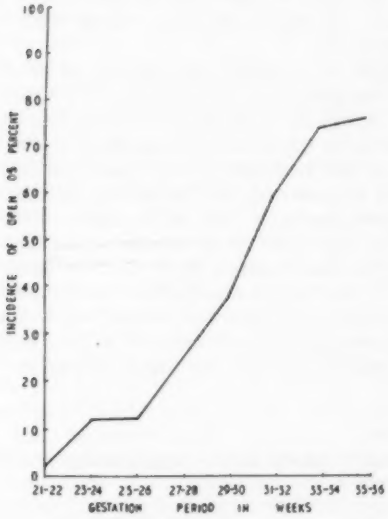


FIG. 1

Incidence of open os at different periods of gestation.

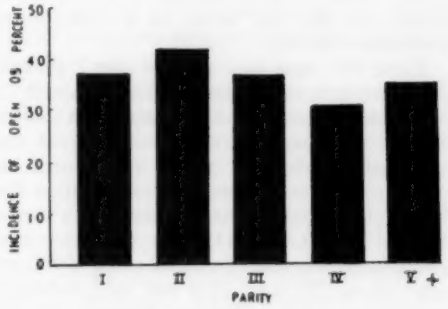


FIG. 2

Incidence of open os in correlation with parity.

increases, the possibility of finding an open internal os progressively rises. Figure 2 correlates the character of the internal os with the parity of the patient and it shows that parity does not affect the character of the internal os.

Out of the 655 patients, 478 were delivered at the Nowrosjee Wadia Maternity Hospital and the remaining 177 did not come to the hospital for their confinement. Amongst these 478 patients, 15 had a premature labour due to certain obvious causes, viz., toxaemia of pregnancy, 7 cases; twin pregnancy, 5 cases; syphilitic infection, 2 cases; and placenta praevia, 1 case. These 15 cases are excluded from further consideration. Thus there remain 463 cases out of which 406 delivered full-term babies whereas 57 had premature babies. The mean duration of gestation and its standard

TABLE II

*Outcome of Pregnancy Correlated with the Character of the Internal Os and with Parity*

| Parity | No. of Cases | Closed Os Cases | | Open Os Cases | |
|---|---|---|---|---|---|
| | | Delivered at Term | Delivered Prematurely | Delivered at Term | Delivered Prematurely |
| I .. .. .. | 75 | 43 | 8 | 16 | 8 |
| II .. .. .. | 103 | 46 | 3 | 43 | 11 |
| III .. .. .. | 72 | 31 | 7 | 31 | 3 |
| IV .. .. .. | 78 | 41 | 5 | 31 | 1 |
| V and above .. | 135 | 71 | 6 | 53 | 5 |
| All .. .. .. | 463 | 232 | 29 | 174 | 28 |

deviation amongst the patients at our hospital is not known. However, the average birth weight of the babies born at our hospital is found to be $5{\cdot}87 \pm 1{\cdot}06$ pounds (Kulkarni *et al.*, 1959). A birth weight of 4 pounds 12 ounces or less was taken as a criterion of premature delivery.

These 463 cases were divided into 2 groups: (1) closed internal os group—261 cases and (2) open internal os group—202 cases. If a patient showed an open internal os at any of the examinations she was placed in the open os group even if at the previous examination she had a closed os. Of the 261 cases with closed internal os, 29, i.e., 11·1 per cent, delivered prematurely whereas of the 202 cases with open internal os, 28, i.e., 13·9 per cent, delivered prematurely. The difference between the incidences of premature delivery in the 2 groups is statistically not significant.

Table II correlates the outcome of pregnancy in the two groups with parity. On statistical analysis, in none of the parity divisions was there found any significant difference between the incidence of premature labour in cases with closed internal os and that in cases with open internal os.

Table III correlates the outcome of labour in the two groups with the duration of gestation at the time of the examination. In cases with closed internal os the duration of gestation at the time of the last examination was taken into account while in cases with open internal os the duration of gestation at the time of the earliest detection of the open internal os was taken into account. On statistical analysis, at no period of gestation at the time of the examination was there found any significant difference between the incidence of premature labour in cases with closed internal os and that in cases with open internal os.

TABLE III

*Outcome of Pregnancy Correlated with the Character of the Internal Os and with the Duration of Gestation at the Time of the Examination*

| Duration of Gestation in Weeks | No. of Cases | Closed Os Cases | | Open Os Cases | |
|---|---|---|---|---|---|
| | | Delivered at Term | Delivered Prematurely | Delivered at Term | Delivered Prematurely |
| 21–24 .. .. | 37 | 27 | 6 | 2 | 2 |
| 25–28 .. .. | 171 | 113 | 15 | 35 | 8 |
| 29–32 .. .. | 161 | 66 | 7 | 75 | 13 |
| 33–36 .. .. | 94 | 26 | 1 | 62 | 5 |
| 21–36 .. .. | 463 | 232 | 29 | 174 | 28 |

## Discussion

It must be mentioned that the repeated vaginal examinations during pregnancy had no harmful effect whatsoever in any of the cases. This is in agreement with Stephens' observation (1958) that previous concern over the use of sterile vaginal examination has proved groundless.

As stated in the beginning, the authors had often found that the internal cervical os allows the passage of an examining finger during the second half of pregnancy. The finding of the present study that nearly one-third of the examinations revealed an open internal os did not, therefore, come as a surprise. However, it is noteworthy that as the duration of pregnancy increases the incidence of open internal os progressively rises. During the 36th week of pregnancy, 49 or 76·6 per cent of the 64 cases studied presented an open internal os (Table I).

The aetiological role of incompetent os in certain habitual abortions during the middle trimester is no longer questioned. A discussion of incompetent os in its various aspects is not intended here. However, it must be emphasized that an open os is not tantamount to an incompetent os. The former merely indicates an anatomical condition which is not necessarily abnormal. The latter means a functional inadequacy which is pathological. The authors can recall many cases with an open internal os in the second trimester of pregnancy which went to full term in spite of a refusal of treatment to forestall a feared abortion. In these cases the open os was not an incompetent one.

We do believe that an incompetent os is responsible for abortions in the second trimester. We had, moreover, often wondered whether there can be any degrees in the incompetency of the internal os. If an incompetent os can cause abortion, is it possible that a lesser degree of incompetency of the os can lead to premature labour? As already shown above, there is no significant difference between the incidences of premature labour in cases with closed os and in those with open internal os. The present study thus reveals the lack of functional significance of an open internal os in the second half of pregnancy and thus discourages a concept of lesser degree of incompetency of internal os. A degree of incompetency of the internal os that would lead to a premature labour does not seem to exist.

## Summary

(1) The internal cervical os during the second half of pregnancy was studied by doing 866 vaginal examinations on 655 patients.

(2) The internal os was found open during 34·6 per cent of the examinations done.

(3) As the duration of gestation increases, the possibility of finding an open internal os progressively rises.

(4) The character of the internal os is not related to parity.

(5) An open internal os during the second half of pregnancy does not lead to a premature labour.

(6) A degree of incompetency of the internal os that would lead to a premature labour does not seem to exist.

## Acknowledgments

Our thanks are due to Dr. K. M. Masani, M.D., F.R.C.S., Honorary Principal Medical Officer, Nowrosjee Wadia Maternity Hospital, Bombay, for his permission to publish this work and to Dr. R. S. Satoskar, M.B., B.S., Ph.D., Assistant Professor of Pharmacology, Seth G.S. Medical College, Bombay, for his help during the preparation of this paper.

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# PREGNANCY ASSOCIATED WITH URETERO-SIGMOID ANASTOMOSIS

BY

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THE association of pregnancy with uretero-sigmoid anastomosis is very rare, the chance of pregnancy being virtually confined to those female cases operated upon for rare congenital abnormalities or for traumatic lesions of the lower urinary tract, who have subsequently remained in reasonable health and attained reproductive age. Lotimer (1954), reviewing the English-language literature, could only find reports of 18 patients who had achieved pregnancy after uretero-sigmoid anastomosis for ectopia vesicae, and Stevens (1941) showed that ectopia vesicae had been the reason for ureteric transplant in almost every case surviving longer than 10 years after operation and reported in the American literature. With improved surgical technique and medical care encouraging longer survival a few more cases may be seen from time to time.

The author's interest in the condition was stimulated by his being confronted with Case No. 1 (reported below) at an antenatal clinic, and two further cases have been found in local hospital records. These are reported in this paper and a review of the literature is made with the object of determining what complications and difficulties may be expected, and arriving at some conclusions about the management of the pregnant patient with uretero-colic anastomosis.

## CASE REPORTS

*Case 1*

Mrs. M. McC. had a bilateral Coffey type uretero-sigmoid anastomosis performed at the age of 7 years for urinary incontinence apparently due to congenital inefficiency of the urethral sphincter. Subsequent health was good and pregnancy occurred at the age of 24 years, and progressed normally until mild pre-eclampsia developed at the 39th week, after which the blood urea level, which was previously normal, rose to 64 mg. per cent. Artificial rupture of the membranes was carried out, and normal labour and delivery produced a healthy infant. There was no evidence of acute upper urinary tract infection during pregnancy or the puerperium and the blood urea level and blood pressure returned to normal in the puerperium. Intravenous pyelography 5 weeks after delivery showed a normal upper urinary tract, and there was not any significant genital prolapse at the postnatal examination.

*Case 2*

Mrs. E. McF., suffered from incontinence of urine of uncertain aetiology from birth, and was treated by bilateral Coffey type uretero-sigmoid transplantation at the age of 18 years. Subsequently occasional attacks suggestive of acute pyelonephritis occurred and at the age of 24 years intravenous pyelography showed "fairly normal left renal excretion and outline with no definite right renal excretion". The blood urea was 74 mg. per cent, the alkali reserve 16·2 m. eq/l. and hypertension of 180/110 had developed. Pregnancy occurred at the age of 25, when the blood pressure had risen to 190/110 and the blood urea 115 mg. per cent, but it terminated in spontaneous abortion at the 22nd week. Following this contraception was advised.

At the time of writing the patient is aged 27 and continues to lead a fairly normal life despite the fact that symptoms of pyelonephritis recur and the blood pressure has risen to 250/120.

*Case 3*

Mrs. M.T.D. acquired an irreparable vesico-vaginal fistula at the age of 20 years during forceps delivery of her first child. Bilateral uretero-sigmoid anastomosis was performed by the Coffey technique when the patient was 21 years old. She again became pregnant at the age of 25 and was delivered of a healthy child by lower segment Caesarean section at term, the indications for abdominal delivery being contracted pelvis and vaginal stenosis due to scar tissue. During pregnancy there were no symptoms of pyelonephritis and the blood pressure was normal throughout. Blood urea estimations were not made. Intravenous pyelography 6 weeks after delivery revealed "slowing of renal excretion and bilateral hydronephrosis and hydro-ureter". The patient became pregnant for the third time at the age of 28, and, after a normal antenatal period, was delivered of a healthy child by elective repeat Caesarean section at term.

At the time of writing the patient is 37 years of age and remains in reasonable health, assisting her husband to manage a farm.

## Special Complications of Pregnancy Associated with Uretero-Sigmoid Anastomosis

Eight complications which might be feared when pregnancy is associated with uretero-sigmoid anastomosis are discussed below. The first five of these complications are directly related to the fact that the ureters are draining into the bowel, whereas the last three are related to the conditions for which ureteric transplantation is commonly undertaken in the young adult or child.

### (i) *Upper Urinary Tract Infection*

*The background of chronic renal infection:* Stevens (1941), in a paper entitled "Longevity Following Uretero-intestinal Anastomosis", mentions 38 patients reported in the literature who had survived for more than 10 years after operation, and, of these, 11 had lived for over 20 years post-operatively. Stevens adds 2 cases of his own surviving for more than 20 years. He concludes from his survey that most, if not all, kidneys whose ureters empty into the bowel become chronically infected after several years, but he comments on the way in which many of these patients with definitely dilated transplanted ureters and probable upper urinary tract infection are able to live for many years with but slowly decreasing renal function. It is interesting to note all except one of these cases of longevity were operated upon for ectopia vesicae.

Pers (1955) investigated the glomerular and tubular function of 15 patients who had undergone uretero-sigmoid anastomosis for a variety of reasons. Using a special technique whereby the clearance rates of intravenously infused penicillin and inulin were measured without collecting the urine, and doing intravenous pyelography on all cases, he showed, by serial examinations, that there was a gradual impairment of renal function, especially that of the tubules. Some degree of hyperchloraemic acidosis, which only occurs in the presence of failing kidneys (Lapides, 1951), was found by Pers in nearly all cases examined more than 4 years after operation. He concludes that slowly progressive chronic pyelonephritis is the determinative factor in the development of renal failure in these cases.

Higgins (1950) suggests that less subsequent renal infection occurs when uretero-sigmoid anastomosis is performed in infancy as the treatment of congenital defects.

*The theoretical increase in risk of renal infection during pregnancy:* The increased incidence of upper urinary tract infection during pregnancy in normal women is thought to be due to urinary stasis invoked by (*i*) ureteric atony under the influence of pregnancy hormones, and (*ii*) ureteric obstruction caused by pressure by the gravid uterus on the ureters as they cross the pelvic brim especially on the right side (Browne and Browne, 1955). Both these aetiological factors will be present when uretero-sigmoid anastomosis is sited at or just below the pelvic brim as is usually the case

(Hinman, 1951). A further obstruction to urinary flow often exists at the actual anastomosis when it is of the Coffey type (Pyrah, 1954). Urinary stasis is, therefore, to be anticipated, and with the constant presence of bowel flora at the ureteric orifices the theoretical chance of a flare-up of renal infection during pregnancy would appear to be greatly increased.

*Assessment of the actual risk of acute renal infection based on case reports:* However, perusal of the literature on the subject reveals that acute upper urinary tract infection is not nearly as frequent as one would expect during pregnancy in these cases. Thus Lotimer (1954) found that of 18 cases in the literature only one (a patient reported by Randall and Hardwick in 1934) suffered from acute pyelonephritis during pregnancy. Lotimer adds a case of his own who had two successful pregnancies and suffered from only one short bout of acute pyelonephritis, which responded promptly to treatment with "Gantrisan" and fluids. Wesolowski and Bulska (1956) report 2 further cases and neither these nor the writer's 3 cases developed evidence of acute renal infection during pregnancy.

Therefore out of a total of 24 cases found by the writer, some of whom underwent more than one pregnancy, there were only 2 reports of flare-up of urinary infection associated with pregnancy; and both of these responded rapidly to simple treatment. This small series suggests, therefore, that, although the incidence of acute pyelonephritis in these cases is higher than the 1 per cent found in normal pregnant women (Browne and Browne, 1955), it is, nevertheless, neither inevitable nor dangerous, and does not constitute a risk sufficient to justify any measures other than careful antenatal supervision, early diagnosis, and prompt treatment in the knowledge that chronic low-grade renal infection is constantly present in the majority of patients whose ureters drain into the bowel.

(ii) *Renal Failure*

Despite the presence of slowly progressive low-grade renal infection in most patients with uretero-sigmoid anastomosis, and the fact that the majority will eventually succumb to renal failure (Stevens, 1941; Pers, 1955), reports of significant renal failure occurring during pregnancy were not found in the literature. It may be that only those with adequate renal function have achieved pregnancy, and their kidneys have therefore had sufficient reserve to cope with the extra work involved: or it may be that pregnancies which have occurred in the presence of definite renal failure have been promptly terminated and thus remain unreported.

In the writer's Case No. 1, the blood urea rose during the last few days of pregnancy associated with signs of pre-eclamptic toxaemia. Case No. 2 had a rising blood urea associated with hypertension in early pregnancy and it is likely that termination would have been required had she not aborted spontaneously. It may be that the literature gives an optimistic impression of the renal function of these cases, and in many the renal reserve may be minimal and insufficient to cope with any additional load imposed by complications such as pre-eclamptic toxaemia. However, most authors agree that, unless marked renal obstruction and infection exist with serious diminution in kidney function, these women should be allowed to bear children (Herman and Greene, 1944; Hinman, 1951; Lotimer, 1954).

(iii) *Pre-eclamptic Toxaemia*

It is surprising that there is no mention of this complication in the literature consulted. Diagnosis depends upon the blood pressure and the presence of oedema, for, though a fairly clear sample of rectal urine can sometimes be obtained, most specimens are not suitable for reliable testing because of faecal contamination. In the writer's Case No. 1 pre-eclamptic toxaemia occurred at term, and in Case No. 2, chronic hypertension was present. Case No. 3, however, maintained a normal blood pressure through two pregnancies.

(iv) *Damage to the Uretero-Sigmoid Anastomosis During Pregnancy or Labour*

Wesolowski and Bulska (1956) regard this as a danger but there is no evidence in the literature that damage to the anastomosis has ever occurred during pregnancy, labour or delivery, and Caesarean section is not indicated on this

account (Herman and Greene, 1944; Lotimer, 1954).

(v) *Damage to the Anal Sphincter During Delivery*

Damage to the anal sphincter causing even slight residual functional impairment might be catastrophic to the continued continence and well-being of these patients. Therefore a wide postero-lateral episiotomy should be made on all cases undergoing vaginal delivery, the wound should be carefully sutured by an experienced operator, and antibiotics prescribed if infection is even suspected.

(vi) *Difficult Labour Due to Vaginal Stenosis*

Vaginal abnormalities are relatively common in these cases because ureteric transplantation has usually been carried out for congenital or traumatic abnormalities. Softening and dilatation sufficient to allow vaginal delivery is to be expected as pregnancy progresses but when a previous traumatic vaginal delivery has occurred, and dense scar tissue or bony disproportion is present, Caesarean section may be required, as in a case reported by Green-Armytage (1933) and 4 cases mentioned by Foda (1959).

(vii) *Subsequent Genital Prolapse*

The high incidence of genital prolapse after pregnancy associated with uretero-sigmoid anastomosis is due to the fact that many of these cases have had ectopia vesicae or other related mesodermal defects with abnormalities of the symphysis pubis and pelvic musculature, and, often, a shorter than normal vagina. Thus 3 of 4 cases reported by Randall and Hardwick (1934) subsequently developed genital prolapse and one underwent anterior colporrhaphy, appendicectomy and uterine suspension between her second and third pregnancies. Morris (1960) mentions a patient who achieved a successful pregnancy after uretero-sigmoid anastomosis and who later had a vaginal hysterectomy and repair performed for procidentia. Nulliparous prolapse associated with ectopia vesicae has also been reported by Clayton (1945) and Randall and Hardwick (1934). Though advocated by Wesolowski and Bulska (1956), few would agree that Caesarean section is indicated merely as an attempt to reduce the risk of a subsequent prolapse which can, after all, be operatively repaired if and when it develops.

(viii) *Transmission of Congenital Defects to the Infant*

Ectopia vesicae and related congenital defects were not transmitted to the child in any of the cases found in the literature. In practice, therefore, this risk may be regarded as negligible.

## Conclusions Regarding the Management of Pregnancy Complicated by Uretero-Sigmoid Anastomosis

By consideration of the points discussed above the following conclusions have been formulated about the practical management of these cases:

(i) *Termination of pregnancy* is not recommended for the condition *per se*, but may be advised if the case presents evidence of significant renal failure.

(ii) *During pregnancy* a copious fluid intake should be maintained and constipation avoided. If a flare-up of renal infection is even suspected the patient should be admitted to hospital for thorough observation, and she should be treated with anti-bacterial drugs unless the diagnosis can be confidently refuted.

The blood urea and plasma electrolytes should be estimated regularly, but there would not seem to be any necessity for radiological examination of the renal tract during pregnancy provided that the blood urea is not grossly raised and calculi are not suspected.

Careful vigilance for any rise in blood pressure or the presence of oedema is required, for pre-eclamptic toxaemia may precipitate renal failure in some of these cases.

(iii) *Labour and delivery* are expected to be normal unless some other complicating factor (e.g., stenotic vagina, bony disproportion, etc.) is present, and they should be managed in the usual way.

However, the anal sphincter and pelvic floor

should be protected by a wide episiotomy whose careful repair and sound healing is particularly important. The presence of uretero-sigmoid anastomosis is not itself an indication for Caesarean section.

(iv) *During the puerperium* a watch should be kept for signs of renal infection, and any pyrexial attacks should be regarded as an indication for treatment aimed at urinary infection (and therefore using anti-coliform agents) unless it is obviously due to some other cause.

The blood urea must be checked during the puerperium, and if it is raised a low protein diet may be prescribed. Intravenous pyelography and other tests of renal function should be arranged if it is thought that they will provide useful information.

As genital prolapse is a common sequela in many of these cases, instruction in suitable pelvic floor exercises should be given, and repair operation may subsequently be required by some patients.

(v) *Contraception or sterilization* must be considered should any signs of renal failure appear, or if the patient requests it after two or more pregnancies. As it has been shown that most of these patients have a gradually decreasing renal reserve it would appear to be advisable for them to limit their families to 2 or 3 children, and to have these over the first few years of marriage before renal reserve becomes grossly diminished.


## Summary

Uretero-sigmoid anastomosis is very rarely associated with pregnancy.

Three cases are reported.

The theoretical risks of this association are presented and discussed in the light of reports from the literature and the progress of the writer's three cases. In practice, pregnancy is reasonably safe in these patients provided it is adequately supervised and there are no signs of actual renal failure when the patient is first seen.

Some conclusions about the management through pregnancy and the puerperium have been formulated.


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# UTERINE DISTENSION AND PRE-ECLAMPTIC TOXAEMIA

BY

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RECENT surveys show that toxaemia of pregnancy is still the most important cause of maternal deaths in obstetrics (Ministry of Health, 1960); it also remains responsible for a tremendous toll of stillbirths and neonatal deaths. The exact aetiology of pre-eclamptic toxaemia is as yet unsolved. In discussing the cause of toxaemia at the International Congress of Obstetricians and Gynaecologists in 1947, Stander and Bonsnes (1949) remarked that "there are enough theories—what we need are more data". The increasing data of the past decade provoked the statement by Kellar (1955) that "the discovery of the cause of pre-eclampsia is probably not far off". This may well be undue optimism, because the aetiology still eludes us. The present communication was prompted by the feeling that any additional new facts, which might throw even some small light on the aetiology of pre-eclamptic toxaemia, should not be allowed to escape unnoticed.

Sophian (1953) propounded the theory that pre-eclamptic toxaemia was due to stretching of the myometrium, producing a utero-renal reflex. He submitted evidence to show that increased resistance to stretching of the uterine muscle produced a reflex inhibition of the renal blood supply, leading to various degrees of renal cortical ischaemia; such ischaemia, he maintained, resulted in salt retention, hypertension and albuminuria. Previously he and Franklin (Franklin and Sophian, 1949) demonstrated this phenomenon in the experimental animal. Goldblatt (1948) showed that hypertension can be produced by renin, a substance produced by renal cortical ischaemia. Dexter *et al.* (1947) found excess amounts of this substance in the renal venous blood of patients with pre-eclamptic toxaemia. In small quantities renin acts as an anti-diuretic (Smith, 1950) and its presence would account for the oliguria encountered in pre-eclamptic toxaemia. There is further evidence in support of Sophian's hypothesis. Tension causes myometrial ischaemia (Reynolds, 1950) as well as a rise in the level of plasma adenosine (Green *et al.*, 1951); the latter substance is also elevated in toxaemia of pregnancy. The isometric tension of the uterus is increased by adenosine (Corner and Csapo, 1953) and reduction of such tension by death or expulsion of the foetus is followed by recovery. On the basis of uterine over-distension, Sophian explains the high incidence of toxaemia in multiple pregnancy, primiparity and concealed accidental haemorrhage. For therapy he adopts measures aimed at relieving the renal cortical ischaemia, and therefore advocates rest, sedation, salt restriction and release of myometrial tension by drainage of liquor amnii or termination of pregnancy.

This hypothesis of Sophian is in many ways plausible and has received much publicity in recent years. It is quoted in most discussions on the aetiology of pre-eclamptic toxaemia. However, we have recently encountered 2 cases of severe pre-eclamptic toxaemia where uterine

distension was non-existent and where this theory is completely untenable. We record these facts because they would seem to show that the utero-renal reflex theory is incorrect and cannot possibly explain the aetiology of pre-eclamptic toxaemia, at least in some cases.

*Case 1*

A.S., aged 36 years, booked at the antenatal clinic on 19th November, 1959, at the 20th week of her 4th pregnancy. She had had 2 live children and her last pregnancy was an ectopic one, for which a salpingectomy was performed at 12 weeks. There was no hypertension or albuminuria in any of these pregnancies.

The patient's blood pressure remained normal (120/70–125/80) and the urine free of albumin until 29th January, 1960. At this stage (32 weeks) she was found to have gained 8 pounds in one month and her blood pressure was 140/85. One week later the blood pressure was 150/100, there was a trace of albumin in the urine and a moderate amount of oedema of the feet and legs. She was admitted to hospital and, in addition to the aforementioned signs, the lie of the foetus was found to be transverse, the haemoglobin was 13 g. per cent and there was no pus in the urine.

The patient was treated by bed rest, chlorothiazide, mecamylamine and serpasil. For 17 days the blood pressure (recorded 4-hourly) remained at about 140/90 and daily catheter specimens of urine contained a trace of albumin. On 22nd February, 1960 (34½-weeks pregnancy by dates and size), the blood pressure rose to 160/100 and the albuminuria increased. The foetus was presenting as a breech. At laparotomy an advanced extra-uterine pregnancy was found; the uterus was lying anteriorly and was soft and slightly larger than in the normal non-pregnant state; the foetus, placenta and membranes were situated in the pouch of Douglas and extending upwards into the abdomen; the presentation was a breech. The amniotic sac was opened and a live male infant delivered, weighing 5 pounds. The pregnancy was associated with the left adnexa—the right ovary and a 3-inch stump of the right Fallopian tube were present. Since it appeared that most of the placenta and membranes could be removed safely, this was done. The puerperium was uncomplicated except for a mild pyrexia, which responded to penicillin. On the 6th postpartum day the blood pressure had fallen to 130/90 and remained at this level until the 12th day, when the patient was discharged. The urine was free of albumin from the 9th postpartum day. The baby was discharged on the 28th day, weighing 5 pounds 10 ounces. Apart from a deformed right foot, the infant was clinically healthy. Postnatal examination on 15th September, 1960: urine, albumin free; blood pressure, 130/80 mm. of Hg; optic fundi, no changes observed in the retinal vessels.

*Case 2*

K.M., aged 27 years, was first seen at the antenatal clinic on 21st July, 1958, at the 22nd week of her first pregnancy. Her blood pressure was 120/70, there was no oedema and no albuminuria. The size of the baby corresponded to that of a 22-weeks pregnancy. Her W.R. was found to be positive on 2 occasions and treatment was given for this. On 21st August, 1958 her blood pressure was 100/60 and again there was no oedema or albuminuria.

On 26th October, 1958 the patient was admitted to hospital complaining of continuous lower abdominal pain for 3 hours. The blood pressure was 150/110, there was oedema of the feet and legs and the urine was laden with albumin. The optic fundi were normal. She was bleeding slightly, dark red blood. The abdominal examination revealed a 36-weeks pregnancy, the abdomen was tense and tender and it was not possible to determine the presentation and position of the child. The foetal heart was heard. The cervix was elongated and tightly closed. An X-ray of the abdomen revealed that the foetus was lying transversely, high up in the abdomen.

On 27th October, 1958 a laparotomy was performed. An advanced extra-uterine pregnancy was found. After incising the sac a live male infant was extracted, weighing 5 pounds 5 ounces. The uterus was now felt (about the size of a 6-weeks pregnant uterus) deep down in the pouch of Douglas. The tubes and ovaries could not be identified, because of adhesions and the overlying sac. As the placenta seemed

quite mobile it was removed without causing undue haemorrhage. The rest of the sac, however, was adherent to bowel and uterus and was left *in situ*.

Apart from a mild pyrexia, which only subsided on the 14th day, the puerperium was uneventful. On the 14th day the blood pressure was 130/80 and, on discharge on the 20th day, 110/65; the albumin disappeared from the urine on the 5th day. The baby was discharged in excellent condition on the 20th day, weighing 6 pounds 1 ounce.

## Discussion

These 2 cases of advanced extra-uterine pregnancy presented the features of severe pre-eclamptic toxaemia. The hypertension, albuminuria and oedema all disappeared rapidly after delivery of the babies by laparotomy. Neither case was seen during the first trimester so that on such a basis it is not possible to say that there was not an underlying essential hypertension. However, there was no evidence in favour of essential hypertension (no fundal changes nor cardiac enlargement) and the rapid disappearance of the signs after delivery is against this. Even if there were a latent underlying essential hypertension (which is most unlikely) then in any case the outstanding feature was the (superimposed) pre-eclamptic toxaemia.

The fact that the pregnancies were extra-uterine and the uterus small with no intra-distension due to a foetus and placenta, shows that pre-eclamptic toxaemia can occur without uterine distension. This is very strong evidence against the uterine distension theory of Sophian with its alleged production of a utero-renal reflex. Such a reflex could not be demonstrated experimentally in dogs by McGaugley *et al.* (1956). Distension of the uterus of the dog does not produce renal cortical vaso-constriction (Abrahams and Pickford, 1958). It has also been suggested that such conditions as over-distension of the uterus in twin pregnancy and uterine stretching against resistance as would exist in primigravidae, reduce the placental blood flow and so lead to hypertension (Browne, 1958). This is also untenable as an explanation in the cases described here.

Further research may throw more light on the problem, but the occurrence of toxaemia in cases of extra-uterine pregnancy would seem to show conclusively that intra-uterine distension is by no means the cause of toxaemia. Such distension may have no bearing on the problem. At the most it may simply be a factor in aggravating a toxaemia or producing it in a few cases. Distension of the uterus may play a secondary role in some cases and then only when the as yet unknown causes of toxaemia are present.

## Summary

Two cases of advanced extra-uterine pregnancy are described complicated by severe pre-eclamptic toxaemia. The toxaemia disappeared rapidly following delivery of the babies.

It is submitted that this is strong, if not irrefutable, evidence against the theory of uterine distension as the cause of pre-eclamptic toxaemia.

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# ACUTE MONOCYTIC LEUKAEMIA IN PREGNANCY

BY

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LEUKAEMIA in pregnancy is rare. Grier and Richter (1939) found 75 reported cases, of which 53 cases could stand critical review. The rest were bibliographical references or not leukaemic. Harris (1953) brought the total to 114 cases.

Very few cases of monocytic leukaemia in pregnancy have been reported. Williams (1948) gave the first description of a case of this type. Harris (1953), while reviewing reported cases of leukaemia in pregnancy, refers to 3 cases of the acute monocytic variety. Two more cases have been described by Gillim (1955).

## CASE REPORT

A Sikh woman, aged 23 years, was admitted to the Military Hospital, Poona, on 12th February, 1960, with complaints of fever, cough, pain in the throat and bleeding from the gums for 5 days. She was a second para. Two years before with her first pregnancy, labour and puerperium had been normal and the child is alive and well. She could not remember the date of her last period. She has not had any illness in the past and there was no relevant family history.

On examination the patient looked pale and ill. Her temperature was 102·4° F., her pulse 110 per minute, and respirations 18 per minute. A few lymph nodes were palpable in the right posterior triangle of the neck. There were patches of congestion with an oedematous base and raised margins all over the buccal mucosa, pharyngeal wall, gums, tonsils and the soft palate. A few of the patches showed central areas of necrosis. There were multiple areas of ulceration on the nasal mucous membrane. Her blood pressure was 110/76 mm. of mercury. The uterus was of the size of a full-term pregnancy with the foetus in the L.O.A. position; the foetal head was engaged and the foetal heart sounds clearly audible. The liver and spleen were not palpable. On the day of admission the total leucocyte count was 288,000 per c.mm. with 91 per cent blast cells. Her haemoglobin was 12 g. per 100 ml. of blood. The majority of leucocytes in the peripheral smear (Fig. 1) were large leucocytes with large oval or round indented nuclei with a reticulated chromatin pattern. Some nuclei were folded. The cytoplasm of some of the cells had a ground glass appearance. Occasional lymphocytes and mature neutrophils were seen. The blast cells were peroxidase positive. The supravital staining showed a few mitochondria and orange granules.

The same evening the patient had a normal delivery of a female baby weighing 6 pounds 4 ounces. The third stage blood loss was not excessive. The cord blood had a total leucocyte count of 19,000 per c.mm. with polymorphocytes 45 per cent, lymphocytes 41 per cent, monocytes 5 per cent, eosinophils 9 per cent and normoblasts 5 per cent.

The placenta was normal for its age with areas of calcification scattered on its surface. The blood vessels within the chorionic villi did not contain abnormal cells but the intervillous spaces contained abundant leucoblasts along with red blood cells (Fig. 2).

The patient was treated with 60 mg. of prednisone a day and 500,000 units of sodium penicillin every 4 hours. In addition 1 in 1,000 potassium permanganate mouth washes and 5 per cent argyrol nasal drops were prescribed.

She had irregular pyrexia. The spleen,

impalpable before delivery, became palpable 3 fingers below the costal margin after parturition and the liver was just palpable. The haemoglobin was 8·3 g. per cent on 22nd February when packed cells from 1 pint of blood were slowly transfused.

On 11th February the sternal marrow showed increased cellularity with rare cells of the granulocytic and lymphoid series. The majority of these cells were blast cells of the monocytic series which were peroxidase positive and showed folding and reticulation of the nuclei. Rare cells of the erythroid series, mostly normoblasts, were also seen.

Her condition gradually deteriorated. On 27th February she had severe melaena. Several dark-coloured, fluid stools without faecal matter were passed. She died the same evening, 2 weeks after childbirth and about 3 weeks after the onset of the symptoms. Permission for autopsy was refused.

## Discussion

Out of the 5 cases of monocytic leukaemia with pregnancy reported in the literature previously, details of 2 cases referred to by Harris (1953) are not available in his article. This leaves 3 cases, one reported by Williams (1948) and two by Gillim (1955) for comparison.

The present case has many features in common with that of Williams. Oral lesions are more common in monocytic leukaemia than leukaemias of other varieties. Both these cases presented with these lesions and irregular pyrexia. Gross splenomegaly, no doubt, was present throughout but was missed before delivery due to displacement upwards of the spleen by the full-term gravid uterus. Allen (1954) drew attention to this possibility previously. Aure (1952), while reporting a case of acute myelogenous leukaemia in pregnancy, states that cortisone had not been tried in these cases. In the present case administration of prednisone did not influence the outcome. Harris (1955) has reported a remission with cortisone in a case of acute lymphatic leukaemia in pregnancy.

Of the two cases reported by Gillim, in one the disease was discovered while the patient was 2-months pregnant. The process was kept under control with supportive therapy and a series of 30 blood transfusions. The patient died 9 months after the onset of disease and 2 months after the birth of a healthy full-term baby. His second case had a more rapid course. The disease started late in pregnancy and the patient died 57 hours after a spontaneous stillbirth. The baby had haemorrhages in the brain but no leukaemic deposits were discovered.

No case of leukaemic infant of a leukaemic mother has so far been reported although congenital leukaemia has been described a few times. No transference of the leukaemic cells across the placenta has been demonstrated in this case or in previous reports (Ohlsson, 1925; Aure, 1952) but animal experiments suggest that it may not be necessary to transport cells to propagate leukaemia. As far as the human cases are concerned, the offspring have not been followed for more than a few years. To arrive at a definite conclusion regarding the effect of leukaemia during pregnancy on the offspring, the children of those leukaemic mothers who were not irradiated as part of their therapy during pregnancy will have to be followed up over a much longer period.

## Summary

(1) A case of acute monocytic leukaemia during late pregnancy is described. The patient died 2 weeks after the birth of a normal infant and 3 weeks after the onset of the symptoms. Cortisone therapy failed to cause a remission of the disease.

(2) A few cases of this type reported in the past have been reviewed and the findings and progress compared with the present case.

## Acknowledgments

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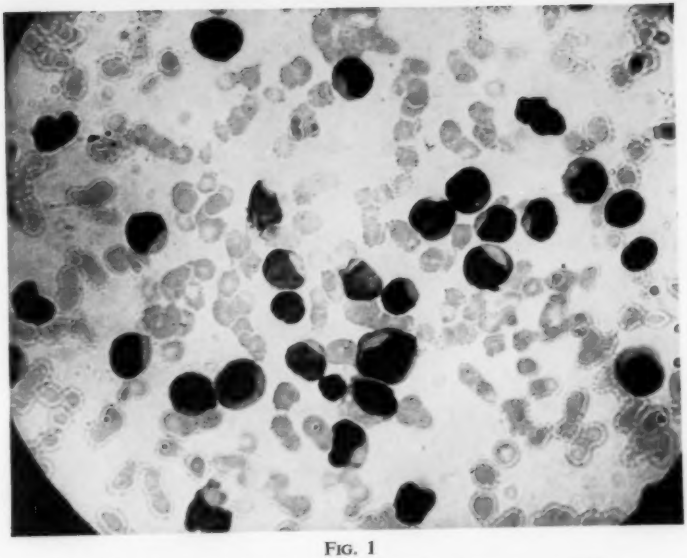

FIG. 1

The peripheral blood smear showing immature leucocytes. ×782.

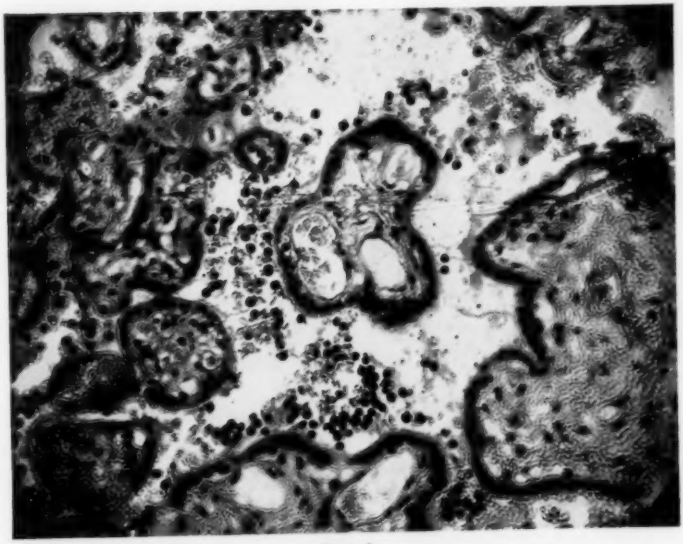

FIG. 2

Microphotograph of the placenta showing large number of leucoblasts in the intervillous spaces. The blood vessels within the villus in the centre of the photograph show clumped red cells but no leucoblasts. ×198.

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# ANTE-PARTUM HAEMORRHAGE DUE TO RUPTURE OF A PLACENTAL VARIX DURING LABOUR

## Report of a Case and Review of the Literature

BY

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THE following case report concerns a very rare cause of ante-partum haemorrhage, not previously recorded in the English literature. Three cases have been traced in world literature, the first from Germany (Rannenberg, 1924) and two, more recently, from America (Leff, 1931; Frech, 1949).

In each of these cases, bleeding had been caused by rupture of a small varix on the foetal surface of the placenta. Only one foetus has survived this accident (Frech, 1949).

### CASE REPORT

Mrs. D.M., aged 26, third pregnancy, unbooked case, admitted to hospital as an emergency, on the 6th August, 1959. Her expected date of delivery was the 20th July, 1959.

*Past Obstetric History*

1955. Spontaneous breech delivery at 43 weeks. Female infant weighing 7 pounds 12 ounces, alive and well.

1958. Spontaneous normal delivery at 43 weeks. Female infant weighing 7 pounds 4 ounces, alive and well.

*Antenatal Care*

This was undertaken by the patient's general practitioner, who mentioned no abnormality apart from varicose veins of the vulva and both legs.

*Investigations*

Haemoglobin estimation, 76 per cent (Haldane). Wassermann reaction, negative. Blood group, "O" Rhesus positive.

*Obstetric History*

The district midwife reported the following sequence of events before admission to hospital:

5th August, 1959—8.30 p.m. Spontaneous rupture of membranes, liquor clear, foetal heart sounds heard, patient not in labour.

6th August, 1959—3.0 a.m. Onset of painful uterine contractions.

5.30 a.m. Sudden painless loss of bright red blood, strong regular uterine contractions, foetal heart sounds not heard.

7.0 a.m. Admitted to hospital as a case of ante-partum haemorrhage.

*Examination*

The general condition was good, blood pressure 130/80 mm. Hg, pulse 90 per minute. There was no demonstrable oedema, nor did an examination of the urine reveal any abnormality.

On examination of the abdomen, the foetus was found to be lying in the right occipito-lateral position, with the head deeply engaged. There was no abdominal tenderness and the uterus was contracting, and relaxing well during the intervals. The foetal heart sounds could not be heard.

Speculum examination of the vagina revealed a slight trickle of blood from the cervix, which was approximately two-fingers dilated. Also noticed at this time was a bulging bag of forewaters, which ruptured spontaneously shortly after the examination, discharging heavily blood-stained liquor. A test for foetal blood was not performed at this time as, unfortunately, facilities were not available. In view of these findings, it was decided to leave labour to progress normally. This resulted in the delivery of a fresh stillborn female infant at 10.40 a.m.

The third stage was completed 10 minutes later, with a further loss of 8 ounces of blood.

The patient's condition after delivery remained satisfactory.

*Examination of the Placenta and Cord*

The umbilical cord showed no gross abnormality. It was 25 inches long and was inserted centrally into the placenta, with no abnormal coiling around the foetus.

The placenta weighed 1 pound 4 ounces. No retro-placental clot or old infarcts were seen. However, the network of veins on the foetal surface of the placenta showed multiple varices of different sizes and shapes. Some were fusiform dilatations of the whole circumference of the vein, others were berry-like sacculations of a small portion of the wall (Figs. 1 and 2).

Injection of the umbilical vein revealed a rupture in one of the fusiform varices, situated 1½ inches from the insertion of the cord (Fig. 2). This had caused extravasation of blood, not only into the amniotic cavity, but also under the amnion.

Histological examination of the placental veins showed no abnormality, other than thinning of the vein wall at the site of each varix.

Post-mortem examination revealed a normally developed female infant weighing 7 pounds 14 ounces. No congenital abnormality was seen and no evidence of exsanguination could be detected.

*Review of Cases*

In the following paragraphs, this case is compared with the three cases previously recorded.

The placenta in each case was of normal size and shape and no retro-placental clots or old infarcts were noted. The umbilical cord was normal and centrally inserted in every case.

The patients' ages ranged from nineteen to thirty. Two were primigravid and two were multiparous. Antenatal progress was apparently normal in all cases and the head was presenting at the onset of labour. Labour commenced at term in two patients and 38 and 43 weeks in the other two. In no case was labour either precipitate or prolonged.

Where the foetus failed to survive, no gross foetal abnormality was noted. The birth weights ranged between 5¾ and 7¾ pounds. Rannenberg (1924) observed that "No anaemia of the internal organs could be detected".

## Discussion

*Differential Diagnosis*

Two rare conditions need consideration, where clinical findings have excluded the more usual causes of ante-partum haemorrhage.

After rupture of a foetal vessel, vasa praevia give an identical clinical picture. This is a much better known condition, described in most textbooks of obstetrics, yet Beer (1954) could only trace 100 cases reported in the previous 180 years.

The second condition is a ruptured vessel of the umbilical cord, not situated in front of the presenting part. In the majority of these cases, bleeding is limited to the umbilical cord, and a haematoma is formed. Occasionally, however, the amniotic coat is torn resulting in bleeding from the birth canal. The literature contains approximately fifty such reports of which less than a quarter have presented as cases of ante-partum haemorrhage.

*Pathology*

Vascular lesions of the large foetal vessels, whether umbilical or placental, have been considered as a whole. The literature available is scanty but it is felt that the pathology must be comparable in all these cases. Four points are considered here, the number and site of the lesions, the nature of any underlying pathology and the reasons for rupture of the vessel wall. Reviewing all the reported cases of umbilical cord haematoma, Dippel (1940) found single lesions in 33 of 36 cases. In the remaining three, two haematomata were present simultaneously, and in each case, they were found to originate from varices of the umbilical vein. In only 3 other cases of this series was the haematoma found to originate from rupture of a varix.

In the case of placental veins, all the lesions were due to varices. A single varix was present in the cases of Leff (1931) and Frech (1949) and in those of Rannenberg (1924) and the writer multiple varices were noted.

In the case presented here 16 varices could be identified with the naked eye on the surface of the placenta, but there was no obvious abnormality of the umbilical vein.

The site of such lesions of the umbilical cord is interesting. Dippel (1940) showed that in 22 out of 29 cases, the rupture occurred near the umbilicus, in 6, near the middle of the cord, and in only 1 was the rupture within 2 inches of the placenta.

In the cases where placental veins were involved, two with single varices were situated 1½ inches from the periphery of the placenta. In the two with multiple varices, only one varix had ruptured and this was situated 1½ inches from the insertion of the cord in each case.

Histological studies of foetal vessel walls, after rupture has occurred, have mostly been done in those of the umbilical cord. Syphilis, degenerative changes, decreased resistance of the wall due to icterus and congenital thinning, have all been blamed for these lesions. Several authorities supported a syphilitic origin, but this was based on a histological picture of round cell infiltration of the cord and in no case was it supported by clinical or serological evidence of syphilis (Dippel, 1940). A similar histological picture was found in 6 per cent of 984 cases in which clinical and serological syphilis had been definitely excluded (Siddall, 1927).

Degenerative changes in the vessel wall have been found histologically only in cases of arterial rupture (Dippel, 1940) and, therefore, need not be considered in these cases.

Decreased resistance of a vein wall due to icterus has only been suggested as a cause on one occasion (Wattersdorf, 1895).

Congenital thinning of the vein wall has been put forward by several authorities. This appears to be the most acceptable theory, as in the 10 cases where varices have been found, 4 in placental veins and 6 in the umbilical vein, no other pathological lesion has been demonstrated in the vessel walls.

Finally, the cause of rupture must be considered, whether the vein wall is diseased or not. It is probable that a normal vessel only ruptures from direct trauma. Such an accident may occur to the umbilical vessels if the cord is short, or entangled around the foetus, or to placental vessels in an abnormal situation, as in cases of vasa praevia.

When a weakened vessel is present, as in the case of a varicose vein, there is a mechanical explanation for rupture. The intra-amniotic pressure in normal labour rises from a resting level of 10 mm. Hg to approximately 24 to 50 mm. Hg during uterine contractions (Caldeyro *et al.*, 1950). The umbilical vein pressure varies from an interval reading of 22 to 34 mm. Hg to approximately 70 mm. Hg during uterine contractions (Haselhorst, 1929).

A healthy vein wall must, therefore, withstand the usual variations in these readings. However, if there is a weakness in the wall, any rise in intravenous pressure may result in rupture at the weakest point of the vein wall. An actual rise occurs during uterine contractions, or in the presence of venous obstructions. A relative rise will be found where rupture of the foetal membranes has reduced the intra-amniotic pressure. This explanation agrees with the theories described below.

Leff (1931) suggested that the integrity of the vein wall was preserved as long as there were comparable pressures on both sides. Therefore, when the foetal membranes ruptured, the sudden drop in intra-amniotic pressure resulted in rupture of the thin-walled varix. In his own case, and those of Rannenberg (1924) and Frech (1941), bleeding occurred when the membranes ruptured. In the case reported here, it may be assumed that the amniotic sac ruptured above the presenting part before the onset of labour and reduction of intra-amniotic pressure was, therefore, more gradual, the varix remaining intact at this stage. Some eight hours after the membranes had ruptured, labour was established and the uterus was contracting strongly. At this point the varix ruptured, due to a rise in umbilical venous pressure without a corresponding increase in intra-amniotic pressure, as liquor amnii was still draining steadily from a high rupture of the sac.

Dippel (1940) supports this theory, but adds that any obstruction to the venous flow may be the precipitating factor in rupture of a weakened vessel wall. Such obstruction may be caused by abnormal looping of the cord around the foetal frame.

FIG. 1

The foetal surface of the placenta, showing multiple varices of the major placental veins and considerable extravasation of blood beneath the amnion.

FIG. 2

An enlargement (×3), of the placental area in which rupture occurred. The site is marked by a collapsed fusiform varix. In a nearby vein, a distended sacculation of the wall is well illustrated.

## Mortality

It is understandable that no maternal death has been recorded in cases of damage to the larger foetal vessels. The foetal salvage rate, however, is extremely poor, the mortality for all lesions being between 50 per cent and 75 per cent even in cases of cord haematomata, where bleeding is limited by the amniotic coat.

Foetal survival in the four cases of placental varices conforms with these figures. When the membranes ruptured before full dilatation of the cervix, no foetus survived. This occurred in the case described and those of Rannenberg (1924) and Leff (1931). The two earlier writers noted that the foetal heart was audible for about five minutes after the bleeding was first detected.

When the bleeding occurred in the case of Frech (1949), the happy coincidence of a fully dilated cervix, sterile obstetric forceps and a competent obstetrician, resulted in the only recorded foetal survival from this condition.

It has frequently been suggested that a simple test for foetal blood should be employed in all cases of ante-partum haemorrhage. In such cases as these, the knowledge that the brisk loss was foetal in origin would certainly help in making a diagnosis but is unlikely to improve the prognosis for the foetus.

In conclusion, it has occurred to the writer that varices of placental or umbilical veins may not be as uncommon as this paper implies. Clearly, the only cases likely to reach publication are those where rupture has occurred. However, a study of the many papers on the foetal vascular system has failed to reveal any record of varices as an incidental finding in an otherwise normal vascular tree.

## Summary

(1) A case of ruptured placental varix is described, causing ante-partum haemorrhage and death of the foetus.

(2) This case is compared with three others in the literature.

(3) The differential diagnosis and pathology are discussed, in association with similar lesions of the umbilical vessels.

## Acknowledgments

I am grateful to Mr. C. W. F. Burnett, M.D., F.R.C.S., F.R.C.O.G., for his helpful criticism and advice, also to Mr. D. Vinten, Medical Photographer, West Middlesex Hospital, for his excellent pictures of the specimen.

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# THE VALUE OF ENDOSCOPY IN THE DIAGNOSIS OF ENDOCRINE DISORDERS

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DURING the last decade new methods of investigation have been introduced for the diagnosis of endocrine disorders. Among these may be mentioned: vaginal smears (Papanicolaou, 1933), cervical arborization test (Paz, 1951), genetic sex determination (Davidson and Smith, 1954), and the various hormone titrations in urine (Jayle and Crépy, 1950) and blood (Forbes, 1950). To these we should now add the endoscopic examinations (coelioscopy and culdoscopy). In the following pages we wish to report our observations in 35 cases of endocrine disorders in which endoscopy has enabled the rapid and accurate diagnosis of the cases studied.

## MATERIAL AND METHODS

The material reviewed here consists of 35 cases who consulted the Rambam Endocrine Clinic for various disorders. The clinical classification of these cases is given in Table I.

Endoscopy was performed by the coelioscope of Palmer (Palmer, 1947). The technique has been described in detail elsewhere (Peretz and Sharf, 1958). It consisted in the examination of the patient under general anaesthesia and in the lithotomy position. The culdoscope was introduced through an opening in the *cul de sac* following a pneumo-peritoneum with $CO_2$ (culdoscopy).

In those cases, where this was not possible (children, virgins, narrow vagina, etc.) the peritoneoscope was introduced through a small incision of the abdominal wall (coelioscopy).

TABLE I

*Endocrine Disorders Studied by Endoscopy*

| Diagnosis | No. of Cases |
|---|---|
| Amenorrhoea, primary | 10 |
| Cases | |
| Hypoplastic ovaries | 3 |
| Male pseudo-hermaphrodite | 1 |
| Agenesis of uterus | 1 |
| Double hypoplastic uterus | 1 |
| Normal genitalia | 4 |
| Amenorrhoea, secondary | 20 |
| Stein-Leventhal syndrome | 4 |
| Ovarian cysts, simple | 4 |
| Atropic ovaries | 2 |
| No pelvic pathology | 10 |
| Intersexes and unknown sex | 5 |
| Malformation of external genitals | 1 |
| Congenital adrenocortical hyperplasia | 4 |
| Total | 35 |

### (A) PRIMARY AMENORRHOEA

In many cases of primary amenorrhoea we are confronted with the question as to the nature of the internal genitalia. It is true that the presence of the gonad could be determined by the examination of follicle-stimulating hormone in urine. However, high values are not always indicative of agenesis of the gonad. In obese

FIG. 1

Mrs. H.M., aged 28. A case of male pseudo-hermaphroditism.

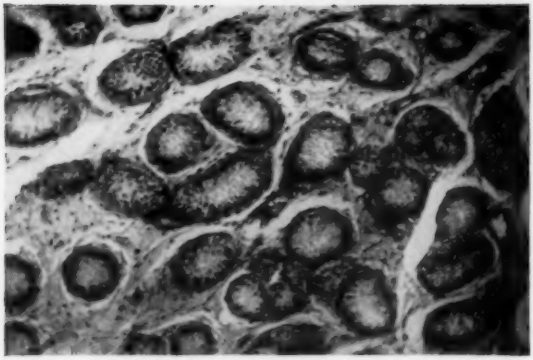
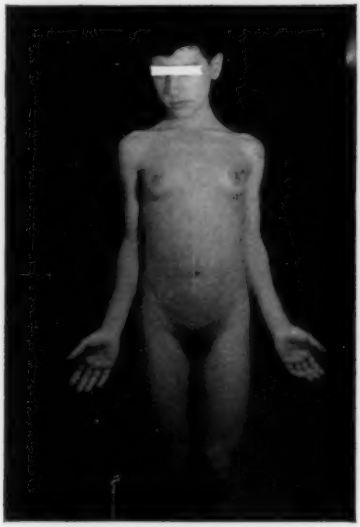


FIG. 2

Mrs. H.M. Biopsy of testes removed from inguinal canal.

FIG. 3

Mrs. B.K., aged 18, suffered from secondary amenorrhoea, obesity and hirsutism.



FIGS. 4 AND 5

P.N., aged 11. Case of agglutination of labia majora. Note breast growth, penis-like protrusion and female pubic hair distribution.

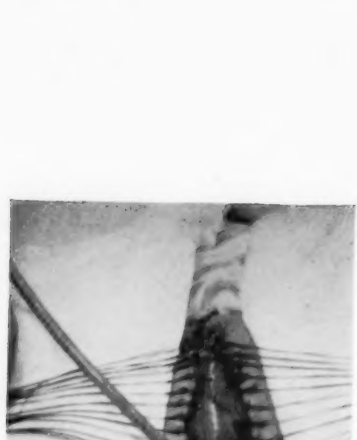


FIG. 6

P.N. View of perineum after separation of labia majora. Normal urethral opening, and normal vagina appeared.

patients and virgins it is sometimes difficult to determine the presence of a uterus. In ten cases of primary amenorrhoea, we were able by endoscopy alone to answer these questions with accuracy and speed, thus obviating various endocrine tests and examinations. It was thus possible to diagnose, among 10 cases of primary amenorrhoea, 1 case of male pseudo-hermaphroditism, 1 case of double hypoplastic uterus, and 3 cases of hypoplastic ovaries probably due to mumps.

The following is an illustrative case of this group:

*Case Report*

H.M., aged 28, married for 2 years, consulted us for primary amenorrhoea. This patient received hormone therapy for about 10 years because of primary amenorrhoea, with no results. On examination (Fig. 1) the patient is a well-developed female, with mature breast development and female hair distribution. Vulva and clitoris were normal. The vagina was about 10 cm. long, ending in a *cul de sac*. On vaginal and rectal examination, it was difficult to determine the presence of a uterus due to the heavy layer of fat. Hormone studies showed normal follicle-stimulating hormone titres pointing to the presence of gonads. Vaginal smears showed marked oestrone deficiency. Other examinations —basal metabolism, 17-ketosteroids, X-ray of sella turcica, sugar tolerance test—were all within normal limits. In order to determine the presence of a uterus and to understand the absence of oestrone secretion with normal follicle-stimulating hormone titres a coelioscopic examination was performed. This examination revealed the absence of both uterus and ovaries. This finding aroused the question of the genetic sex of the patient. Skin biopsies and leucocyte examination showed male genetic sex. Following this finding, a meticulous search revealed two small testes in the depth of the inguinal canal. A unilateral orchidectomy confirmed the diagnosis of male pseudo-hermaphroditism (Fig. 2).

(B) Secondary Amenorrhoea

The classification of 20 cases of secondary amenorrhoea studied by peritoneoscopy is given in Table I.

Of the cases with secondary amenorrhoea there were: 9 cases in whom the amenorrhoea was associated with obesity and hirsutism. In these cases we had to differentiate between (1) polycystic ovaries, (2) arrhenoblastoma and (3) adrenocortical hyperplasia. Culdoscopy was of vital importance in the diagnosis, especially when the values of 17-ketosteroids were in the upper limits of normal. The following case is characteristic:

*Case Report*

B.K., aged 18. Since the age of 13 the menses occur every 6 to 8 months. During the last 2 years there has been a marked development of hirsutism on face, abdomen and gluteal region (Fig. 3). The clitoris was enlarged. During the last 12 months the patient gained 8 kg. in weight. On rectal examination it was difficult to determine the condition of the genitalia due to the heavy layer of fat. Laboratory examination showed normal follicle-stimulating hormone secretion. The vaginal smears revealed moderate oestrone activity. The 17-ketosteroid secretion was 17·5 mg. per day. The Wilkins suppression test did not reveal a definite lowering of 17-ketosteroid excretion. This suggested the possibility of arrhenoblastoma. On culdoscopy the ovaries revealed features characteristic of the Stein-Leventhal Syndrome, thus enabling a definite diagnosis. Wedge resection of ovaries was then performed, with subsequent regular menstruation.

(C) Sex Determination

There were 5 cases in whom it was difficult to establish the gonadal sex of the patient on clinical examination alone. These were children of varying ages. (We are grateful to the Paediatric Department, Rambam Hospital, for sending these cases to us.) In 2 of these cases the laboratory tests pointed to adrenocortical hyperplasia. There was one case which presented a different problem:

*Case Report*

P.N., a boy aged 11, was brought to us because of growth of both breasts that started at the age of 10. The mother reported that the boy was born with a small "penis" and non-descended

testes. The boy grew up as a male, although he preferred to play with girls and would urinate in the sitting position. At the age of 10, pubic hair growth began and breasts started to develop (Fig. 4). The boy received varied hormone therapy with no effect on his psychic attitude or breast growth. Hormonal studies showed 17-ketosteroids 1·2 mg. per day and urinary oestrogens 25 mg. per litre. On the basis of these findings it was suggested that the boy undergo an exploratory operation on both adrenals because of the suspicion of a hormone-producing tumour.

The family refused this procedure but subsequently attended our clinic. On examination we found that the boy's "penis" consisted of a 3 cm. long protuberance with a hypospadic opening. The perineum was flattened out with a thicker and darker skin. No gonads were palpable. Blood smear for genetic sex determination showed the "boy" to be a female. In view of this finding coeloscopy was performed. A normal uterus, tubes and ovaries were seen. It was clear that the girl had at least two-thirds of her upper vagina. This brought up the diagnosis of adhesion of the labia majora with the secondary formation of a protuberance through which the urine was passed (Fig. 5). We then carried out a separation of the labia by dissecting the raphe (Fig. 6) in the midline of the perineum. On separation a normal vulva, hymen and vagina were found. This case illustrates how coelioscopy leads to a rapid and precise diagnosis.

## Discussion

In the diagnosis of various endocrinopathies, an exploratory laparotomy, no doubt, facilitates the diagnosis as, for example, in the Stein-Leventhal syndrome, intersexes, agenesis of ovaries, etc. However, it is seldom that we resort to this type of investigation, for obvious reasons. It is here that the major role of coelioscopy or culdoscopy is shown. The ease with which it is performed, the lack of complications and the definite information that is obtained give this method of examination a definite role in the diagnosis of endocrinopathies (Jeffcoate, 1960). There is little substitute for direct vision of the genitalia in the diagnosis of many equivocal cases. Endoscopy is essential in children or young girls, where examination of the pelvic organs is not possible.

## Summary

The abdominal coelioscopic or culdoscopic examination in the diagnosis of endocrine disorders is essential for precise and rapid diagnosis. The results of our experience in 35 cases of amenorrhoea, hirsutism, intersexes, etc., are reported above. The details of 3 illustrative cases are reported. The ease in performing this examination, the lack of complications and the precise visual picture of the pelvic content, offer an invaluable method in various types of endocrine disorders.

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# CONGENITAL ABNORMALITIES OF THE UTERUS AND ASSOCIATED MALFORMATIONS

BY

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SOME degree of doubling of the reproductive tract is present in most mammals. Duplication in the human is seen in the Fallopian tubes, but incomplete fusion of the paramesonephric (Müllerian) ducts during the 3rd and 4th months of foetal life may lead to varying degrees of bipartite uterus and vagina. Malformations of the uterus have long been known to be associated with abortion and prematurity (Eastman, 1956). It has been suggested that an undue proportion of aborted and post-28-week foetus are malformed. The available evidence in the literature is, however, not convincing on the latter fact.

In explanation it is usually assumed that implantation is abnormal. However, Holmes (1956) reported a female stillborn child who had a slight degree of bifid uterus with one cervix. This child was born to a mother with a severe degree of bifid uterus. Stevenson, Dudgeon and McClure (1959) reported the same phenomenon in two other mothers and female children. It seems possible therefore that some dominant or multiple genetic factors may determine inheritance of bifid uterus.

The frequencies of all and of specific degrees of this malformation are very difficult to determine. A series such as the one reported below and those of Holmes (1956) and Blair (1960) selects mothers who become pregnant and who carry at least one child sufficiently long to be admitted to a maternity hospital. In such women it would appear that the condition is recognized in between one and two per 1,000. In Belfast four women had some degree of didelphys in 983 consecutive cases of abortion (Stevenson, Dudgeon and McClure, 1959).

However, both in maternity hospitals and in abortion series the true frequency is almost certainly higher, as unless there is a double cervix slighter degrees are probably not always recognized and the condition is sometimes obvious only at Caesarean section. It can be missed even then. There probably are, however, many women so affected who only have abortions and the condition is also encountered in infertility clinics, but it does not seem to be present in more than a small proportion of women investigated for study by uterosalpingography.

Perhaps the best overall rough estimate that can be made is that in one or two per 1,000 women there is malformation of the uterus of sufficient degree to hazard a pregnancy.

## PRESENT INVESTIGATIONS

Between January, 1950 and December, 1958 in the United Oxford Hospitals beds in the Area Department of Obstetrics and Gynaecology, Oxford, 15,967 mothers were delivered. The condition of didelphys was noted in 36 of

these mothers or in about 3 per 1,000. No doubt there was some selection for admission because of previous abortions, malformations and other relevant reasons, but as some 60 per cent of all mothers in the district are confined in hospital and not all cases are recognized, it would seem unlikely that fewer than 2 women per 1,000 even in those who carry a child to 28 weeks have bifid uterus in some degree. Of these 36 mothers, 24 have been interviewed. Most of them were confined in the early part of the period. There is some relevant information about all these mothers, but considerably more concerning the 24 who were traced. The latter were visited and a family history obtained, relations being seen as appropriate.

### Other Anomalies in the Women with Bifid Uteri

Many writers have called attention to the association of malformations of the uterus and anomalies of the organs developed from the urogenital ridge. These have been reviewed by Jarcho (1946) and Woolf and Allen (1953). Failure of the development of one uterine duct is commonly associated with renal agenesis on the same side. Ureteric constriction may occur. Horse-shoe kidney, pelvic kidney and hypoplastic kidneys with varying degrees of fibrous and cystic degeneration have been described. The case may present with bouts of lower abdominal pain.

Of the 24 women in this series who were traced, only 4 had had suspicious histories; they appeared to have had only relatively mild infection of the urinary tract.

### Menstrual History

Dysmenorrhoea and menorrhagia are supposed to be associated, but the present series is not large enough to give adequate data. Three mothers said that they had had severe dysmenorrhoea before their first pregnancy and three had menorrhagia at the time of interview. One woman with bicornuate uterus had noticed that alternate periods were always much less severe. Clearly such figures cannot be interpreted.

### Degrees of Didelphys

Of the 36 women ascertained:

19 had bicornuate uterus with horns of about equal size, and a single cervix;

4 had bicornuate uterus, double or incompletely fused cervices and septate vaginae;

3 had bicornuate uterus with one cervix but one uterine horn was very small;

5 had uterus subseptus and 5 had arcuate uteri.

### Reproductive Performance of the Women with Bifid Uteri

Ages at marriage ranged from 16 to 32 years. Dates of marriage can be compared with dates of conception in 22 of the 24 women who were interviewed. Fourteen conceived within a year of marriage, 4 conceived within 2 years, and one each within 4, 6, 8 and 11 years of marriage. There is no obvious relationship of the delay in conception with type of malformation of the uterus, the women with delays of 4, 6, and 8 years all had bicornuate symmetrical uteri and the delay of 11 years was associated with arcuate uterus.

### Outcome of Pregnancies

These are summarized in Table I. Of 117 pregnancies 27·3 per cent ended in abortion. Of mature births 9·4 per cent were stillborn and of all mature births 6·1 per cent were malformed. The frequency of abortions was particularly high in first pregnancies. Of these 14 out of 36 or 38·9 per cent ended in abortion.

In 17 cases the duration of the abortions was less than 12 weeks.

### Complications of Pregnancy and Labour

The major complications were, in pregnancies which advanced beyond 28 weeks, malpresentation 30 (of these 20 were breech); ante-partum haemorrhage 9; post-partum haemorrhage 5; retained placenta 11; 5 cases were delivered by forceps and 13 by Caesarean section.

TABLE I

*Outcomes of Pregnancies*

| | Live Birth | | Stillbirth | | Abortion | Total |
|---|---|---|---|---|---|---|
| | Normal* | Abnormal* | Normal* | Abnormal* | | |
| 24 women (interviewed) .. | 52 | 2 | 4 | 1 | 23 | 82 |
| 12 women (not traced) .. | 22 | – | 2 | 2 | 9 | 35 |
| Total .. .. .. | 74 | 2 | 6 | 3 | 32 | 117 |

* As recognized at birth.

### MALFORMATIONS IN OFFSPRING

Of 85 post-28th week pregnancies, 5 resulted in foetus recognized as malformed at birth. These malformations included (one instance each): abnormal genitalia; atrophic testis; talipes; deformity of knees; persistent foetal alignment of both hips; deformity of sternum; cleft palate. The post-mortem reports on two male infants described in one case polycystic kidneys together with hypertrophy of the circular muscles at the junction of the ureter with the bladder, the other male child had a hypertrophic bladder.

During this period in the hospital ward the total number of deliveries which ended in at least one malformed child was 310 or 1·94 per cent of all deliveries.

However, the malformations recognized later are perhaps of particular interest in that they suggest that a tendency to maldevelopment of the urogenital ridge is inherited by children of these women.

### TWO GENERATIONS

The mother, C.H., with double uterus, double vagina and 2 cervices, had one abortion and 6 subsequent live births including one set of twins (6th pregnancy, male and female, one in each horn) (Fig. 1). Both twins were delivered by the right cervix, the left cervix remained undilated, the placenta was in the right horn. She had experienced during her pregnancies ante- and post-partum haemorrhages, also infection of the urinary tract.

One child (3rd pregnancy) was found to have testicular atrophy. One daughter (4th pregnancy) at the age of 14 complained of dysmenorrhoea but was too young to be submitted to fluoroscopic examination, and on rectal examination no gross abnormality was found. Another daughter (5th pregnancy), seen at the age of 13, had suffered during the past few months from severe attacks of lower abdominal pain; an intravenous pyelogram showed a right-sided hydronephrosis due to ureteric constriction at the uretero-pelvic junction of the kidney.

In the family pedigree, the father had twin brothers.

Another mother, S.C., had a bifid uterus with horns of about equal size and a single cervix as shown by salpingogram (Fig. 2).

She gave a history of ante-partum haemorrhage. Her 7 pregnancies had included 2 abortions, 2 stillbirths (one male with malformation of genitalia), and 3 single births with breech presentation (one of the latter was a girl with persistent foetal alignment of both hips, later corrected by osteotomies of both femorae and tibiae). In the family history an elder sister of this mother had had twins.

### INFORMATION ABOUT RELATIVES

One woman remembered that her mother mentioned having an abortion, or dry labour and bleeding. The mother of another had 3 days after childbirth passed a "false birth". One sister suffered from "kidney trouble". One sister and a niece both had club feet.

### TWINNING

No history of consanguinity was obtained between a woman and her husband. Amongst the 36 cases 3 women had twins, amongst

siblings one case of twins on the woman's side, 4 on the husband's. In more distant relatives there were 4 cases of twins on the husband's side, 9 on the wife's. Of triplets, one instance each was recorded among the wife and the husband's relatives.

Of the 15,967 deliveries between January, 1950 and December, 1958, 352 resulted in twins giving a rate of 22·05 per 1,000 deliveries.

When twins occur in a woman with both double uterus and double vagina, one birth may precede the other by several days (Kennedy, 1959).

### Bifid Uteri Described Post-mortem

During the period under review records in the Pathological Department, Radcliffe Infirmary, Oxford, mentioned that two middle-aged women who had suffered from severe uterine haemorrhages, had bifid uteri; another woman aged 73, a case of bronchopneumonia, was found to have both double uterus and double cervix. Details were also available of 4 neonatal deaths with numerous deformities including bifid uterus; one of the mothers had hydramnios, and there was a stillborn infant with many congenital defects including uterine malformation, whose mother's pregnancy had been complicated by uterine fibroids.

### Genito-urinary Abnormality in Children

The records of 28 cases of congenital malformation of organs developed from the urogenital ridge treated in the Children's Department, Radcliffe Infirmary, Oxford, between 1948–1957 included 9 instances of re-duplication or ureter and 5 of the kidney. Visits were paid to the homes of 9 of these children 4 of whom had double ureters. In the obstetric histories of the mothers there had been no abortions and most deliveries had been spontaneous. In the family histories there were 5 instances of twinning on the maternal side.

### Conclusion and Summary

The data given in this paper suggest that the clinical appreciation of congenital malformations in organs developed from the urogenital ridge, which may influence a woman's reproductive life and the well-being of her children, is made more difficult by the different forms in which these anomalies may present.

Studies of the natural history of 36 women with congenital abnormalities of the uterus have shown that the outcome of the 117 pregnancies of these women up to July, 1959 has been as follows: abortion 32 (27·3 per cent), stillbirth 9 (9·4 per cent). Malformations were noted in 3 of the stillborn and in 2 of the live births, thus of 85 mature births 6·1 per cent were malformed. Malpresentation occurred in 30 cases (35·3 per cent); ante-partum haemorrhage 9 (10·6 per cent); post-partum haemorrhage 5 (5·9 per cent); retained placenta 11 (12·9 per cent). Caesarean section was carried out in 13 cases (15·3 per cent) in comparison with a 5·8 per cent overall incidence for the same period in the United Oxford Hospitals beds.

It would seem therefore that there is a considerably higher risk to the mother with didelphys and to her offspring. There was high foetal wastage in terms of early or late loss and malformation in these women.

It has to be remembered that the maternal data were ascertained during pregnancy, some discovered following an untoward result in pregnancy. However, the condition was discovered in 19 women at routine antenatal examination in first pregnancy or subsequently at examinations not determined by previous labour difficulties or untoward outcomes.

Present lines of thought concerning the aetiology of malformations present at birth and not determined by single mutant gene mechanisms suggest that intra-uterine environment and genetic predisposition both contribute to a majority of malformations. The condition of didelphys is of particular interest in that it seems likely that a relatively simple form of inheritance may determine the specific anomaly of a degree of didelphys in the child while the probable excess in other malformations suggests that something related to the usual uterine environment for the species, perhaps implantation anomalies, is responsible. Thus congenital but non-hereditary and hereditary anomalies may be associated in a unique way.

FIG. 1

C.H. Twin pregnancy suggested on X-ray investigation of 6th pregnancy. A foetus is displaced to either flank and tends to be held vertical in that position.

FIG. 2

S.C. Salpingogram. Bicornuate uterus, both tubes are patent.

## Acknowledgments

Dr. A. C. Stevenson initiated this enquiry and throughout sustained it by helpful criticism.

We are very grateful for the assistance of Miss J. R. Barnett and Miss K. Major, Health Visitors attached to this Unit, in home visiting.

The X-ray Department, The Radcliffe Infirmary, Oxford, helped us with photographs. Dr. Victor Smallpeice kindly made available information about certain paediatric cases.

Thanks are due to the Records Department, The Radcliffe Infirmary, Oxford, for facilitating access to the case sheets and are also due for much help to the Statistical Department, Oxford Regional Hospital Board.

We wish to acknowledge the co-operation of individual family doctors in the contacting of their patients.

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# THE USE OF PROSTIGMINE IN THE HEARTBURN OF PREGNANCY

BY

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HEARTBURN is one of the common minor afflictions of pregnancy. It frequently responds to simple treatment with alkalis and sleeping in the semi-erect position, by diminishing acidity and discouraging oesophageal reflux. However this line of treatment fails in a minority of patients and the symptoms can then become something of a trial.

Opaque-meal X-ray examination of the upper alimentary tract in pregnant patients suffering from severe heartburn showed (Gomez-Sigler, 1947) that of 137 patients 79 had a normal motility pattern, the remaining 58 exhibiting slow filling and decreased motility. From these observations arose the idea of treating refractory heartburn of pregnancy with prostigmine, by intramuscular injection (Gomez-Sigler, 1947; Sullivan, 1950) or orally (Wiley, 1946) with encouraging results on direct trial.

In the present instance it was decided to run a blind trial. Women attending Oldchurch Hospital antenatal department were asked if they suffered from heartburn—this was done as it was found that the patients almost never complained spontaneously of this symptom, thinking that it was a normal phenomenon which must be tolerated. The patients who failed to obtain relief with antacids were the subjects of the trial. Enquiry was continued until 100 patients had been collected.

The pharmaceutical department put up 100 ampoules marked with 100 different figures in a random manner so that the contents were unknown to the obstetric staff. Fifty ampoules contained water and 50 ampoules 0·5 mg. prostigmine. The contents of the ampoules were given intramuscularly and the results evaluated. Later the key to the ampoules was obtained from the pharmacy and the results correlated. The relief obtained was classified as follows:

| Group | Patients Given Prostigmine | Patients Given Water |
|---|---|---|
| A. (complete relief of symptoms) .. .. | 17 | 12 |
| B. (useful relief, but slight residual symptoms) | 21 | 8 |
| C. (injection useless) .. | 12 | 30 |

Groups A and B were considered to have obtained a useful result, giving the following table:

| | Prostigmine | Water |
|---|---|---|
| Useful result .. | 38 | 20 |
| Useless result .. | 12 | 30 |

Statistical analysis of these figures gives a figure for $\chi^2$ of 13·30 corresponding to P less than 0·01, i.e., a highly significant result.*

From the trial 76 per cent of the patients given prostigmine and 40 per cent of those given water obtained useful relief.

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* $\chi^2 = \frac{(38\times30-20\times12)^2\,(38+20+12+30)}{(38+12)\,(12+30)\,(30+20)\,(20+38)}$

$= \frac{(900)^2\,(100)}{50\times42\times50\times58}$

$= 13{\cdot}30$

No. of degrees of freedom (n) is 1.

Hence P is less than 0·01.

Patients with alkali-resistant heartburn can therefore be divided into three groups:

(*i*) 40 per cent who received relief from water injection—presumably with some psychological basis;

(*ii*) 36 per cent (i.e., 76 per cent–40 per cent) who obtained relief from prostigmine but not from water;

(*iii*) 24 per cent (i.e., 100 per cent–76 per cent) who obtained no relief from either water or prostigmine.

The results of this trial suggest that an injection of prostigmine would relieve some three-quarters of patients unrelieved by antacids, about half of them by suggestion and half of them by a genuine pharmacological action. It seems therefore that the drug deserves a definite place in the obstetrician's armamentarium—probably considerably wider than it at present enjoys.

The average duration of relief obtained from an injection was 5 days. No side-effects were noted.

I wish to express my thanks to Mr. John Watt for permission to run this trial in his department, to Dr. M. P. Curwen for checking the statistical results and helpful suggestions, and to the pharmaceutical department of Oldchurch Hospital for making up the ampoules.

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# STRANGULATION OF THE UTERUS CAUSED BY A RING PESSARY

BY

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STRANGULATION of the uterus is a rare condition, and very few cases are reported in the literature. The present case report concerns a patient whose uterus prolapsed through her ring pessary, and became strangulated.

## LITERATURE

Several instances of strangulation of a procidentia are recorded. These are due to various causes, and generally associated with infection. The type of case in which it becomes difficult to reduce a procidentia is not uncommonly encountered, and an early record of such a case is that of Slocum (1889). He describes the case of a negress whose prolapse of many years duration suddenly became irreducible. It was successfully treated by posture, using the knee-chest position.

Beyea (1898) reported a case of strangulation of the uterus following complete prolapse, accompanied by infection, in a young woman of 22 who had 4 children. In this case the prolapse had been irreducible for 4 years, and on admission the main feature appeared to be infection of the procidentia; there was no abdominal distension at the time. The patient was treated by vaginal hysterectomy, and subsequently died. The uterus contained multiple abscesses in the myometrium.

Baldy (1898) reported a case in a woman of 70. In this case the uterus, which contained fibroids, was irreducibly prolapsed, and became strangulated. Reposition was accomplished, and abdominal hysterectomy performed. The patient recovered.

Von Jaschke (1929) described a case of irreducible procidentia where the patient finally recovered following gangrene and sequestration of the major portion of the uterus. He observes that in the majority of cases death results whether the patient is treated operatively or conservatively.

Holden (1935), in a discussion on the use of colpectomy in the treatment of prolapse, mentioned the case of a patient with irreducible procidentia. She was treated conservatively for 48 hours, the procidentia was then reduced, and the ulceration healed after a further 2 months. Holden mentioned 3 other cases of irreducible prolapse, all of whom died of sepsis.

Frank (1938) reported a case of strangulated procidentia in a woman of 42. She had 2 children, and the last pregnancy was 10 years previously. For one year she had suffered from uterine prolapse, but this had always been reducible. Two weeks prior to admission to hospital the prolapse became irreducible, and when finally admitted there was evidence of intestinal obstruction. All attempts at reposition failed, and the condition was treated by laparotomy with decompression of the distended bowel, aided by pressure applied vaginally. The patient made a good recovery, and had a formal operation for the treatment of her prolapse in due course.

A case of intestinal obstruction associated with complete procidentia was reported by Daley and Callum (1946). They described a complete procidentia in which ulceration of the posterior fornix had occurred, allowing a large loop of small intestine to be extruded; the

FIG. 1

This shows the oedematous procidentia, with the watch-spring pessary which had caused strangulation. The spring consisted of eleven steel bands.

FIG. 2

Showing the recovery of the vaginal mucous membrane 17 days after division of the ring pessary.

bowel had subsequently become strangulated.

Svesko (1958) described the use of total colpectomy in the treatment of irreducible uterine procidentia in a multiparous patient of 81. Preliminary attempts at reposition had completely failed, although the patient's general condition did improve and there was no obstruction to the intestinal or urinary tracts. She made a good recovery.

## Case Description

The patient was a woman aged 48, the mother of 2 children, who had suffered from a marked degree of uterine and vaginal wall prolapse for 12 years. During this time she had not sought active treatment until a month prior to admission. She was then found to have a procidentia; this had been reduced by her own doctor, and a watch-spring pessary inserted.

All was well until the morning of the day of admission to hospital, when the patient found that it was difficult to pass urine. She became steadily more uncomfortable, and at 4 p.m. she noticed a swelling appearing at the vulva. By now she was completely unable to pass any urine, some vaginal bleeding was noticed, and she experienced severe lower abdominal pain.

Later the same evening the patient was admitted to the Bristol General Hospital as an emergency. She was found to have a large irreducible procidentia, bluish-black in colour; at its base the procidentia was constricted by a Number 8 watch-spring pessary. She was in great pain, but there was no abdominal distension, nor was there any evidence of a distended bladder. It was evident that the procidentia contained not only uterus, but bowel and bladder in addition.

A general anaesthetic was given and, with considerable difficulty, the watch-spring pessary was divided. In this process, various instruments were tried with only partial success, notably a Gigli saw, and a wedding ring remover, both of which soon broke. The ring was finally divided with a strong pair of bone-forceps.

Following division of the ring, no attempt was made to replace the procidentia; the vaginal mucosa was so friable and oedematous that it would have been seriously damaged by any such pressure. A catheter was inserted into the bladder, and a few millilitres of blood-stained urine were withdrawn. It was evident that the ureters had been compressed, and that the patient suffered from anuria, and not from retention of urine.

The catheter was left *in situ*, and connected to a continuous suction drainage system. The procidentia was covered with vaseline gauze dressing, and the patient's general condition was closely observed. The pulse rate was at first in the region of 120 per minute, but gradually over the course of 3 days it slowed to 84 per minute. A low-grade pyrexia was present throughout the first 3 weeks of the patient's stay in hospital.

The urinary output improved dramatically, the blood-staining lessened, and within 24 hours the urine was normal. Bowel sounds had been absent on admission, but re-appeared within a few hours of the division of the ring pessary.

During the first week the vaginal mucosa looked as if it was about to slough in one area. In fact, it remained intact and gradually recovered. By the 10th day after admission the vaginal mucous membrane had recovered sufficiently to allow reposition; this was accomplished without difficulty, and without anaesthesia. Further local treatment with flavine packs helped to keep the prolapse in place, and cleaned the vagina in readiness for operation. It was a month from the day of admission before the patient's general condition was entirely normal again.

Two months after admission vaginal hysterectomy was performed, together with repair of a large enterocele, anterior colporrhaphy and colpo-perineorrhaphy. The actual operation presented no special difficulty nor were there any residual signs of the previous strangulation. A course of antibiotics was given, and also a blood transfusion of 2 pints in view of anaemia; the patient made a good recovery.

## Comment

When strangulation of a procidentia occurs the main dangers are infection and damage to the intestinal and urinary tracts. No other record has been found in the literature of strangulation caused by a ring pessary, and in

that respect the case reported appears to be unique.

The condition of strangulation of a procidentia carries a high mortality, and the initial period of conservative treatment, to allow natural recovery of the tissues, played a large part in the successful outcome of the case.

## Acknowledgments

I should like to express my thanks to Professor Gordon Lennon for permission to publish this case, to Miss Audrey King for her kind assistance, and to the University of Bristol Department of Medical Photography for the illustrations.

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# VESTIBULAR ANUS

## A Report of 2 Cases

BY

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REPORTS on vestibular anus such as the one by Wright in 1947 and other related papers by Robertson (1949), Moore and Lawrence (1952), Powell and Lowden (1953) and Gordon Millar and Black (1955) on fistulous openings between the lower end of the gut and any part of the vulvar region are valuable contributions to practical aspects of embryology. Ladd and Gross (1941) described these abnormal communications between the rectum on one hand and the bladder, the urethra, the uterus, the vagina or the perineum on the other as various types of fistulae associated with imperforate anus.

As the anatomical description of the area referred to as the vestibule differs widely the term vestibular anus could be considered a pardonable misnomer to describe any one of the above conditions. That this condition is not infrequently met with in local gynaecological practice is shown by the fact that 4 such cases, all in the child-bearing period, were admitted to this hospital in the last 3 years. The first 2 cases came under care for infertility. This, the third case, was seen at full-time pregnancy while the fourth case was admitted mainly for the relief of this abnormality.

The last 2 cases who were treated during 1960 are being presented here, with a description of the management at the time of delivery in one and of the surgical correction of the deformity in the other.

*Case 1*

B.B. (3342), *aet.* 20, a primigravida, was admitted on 18th March, 1960, early in labour. Abdominal palpation revealed a full-time uterus which was acting moderately.

On inspection of the pudenda, the anus was absent at the normal site but was found to be opening just above to the fourchette. There was no dimpling of the skin in the area where the anus ought to have been. The patient was apparently aware of the deformity. But she did not seek medical advice prior to this as she had not experienced any inconvenience.

A vaginal examination showed a well-effaced cervix and an os dilated up to 4 cm. The vertex was engaged and the pelvis was found to be adequate. The anal orifice felt patulous to the examining finger though bowel control had been satisfactorily maintained by the action of the pelvic floor muscles. In order to avoid injury to the anal margins and the levator ani a lower segment Caesarean section was performed under spinal anaesthesia and a vigorous female child weighing 6 pounds was delivered. The patient did not develop any pyrexia that could be attributed to the abnormal situation of the anus. She was discharged well with her baby on the 15th post-operative day.

*Case 2*

L. (9534), *aet.* 24, was admitted on 21st July, 1960, complaining of infertility and certain

marital difficulties. On further enquiry she said that she had been examined elsewhere and informed of some malformation in her genital tract. At this her husband became gravely concerned and brought her to Hyderabad. Her bowel control was said to be good except when she had an attack of diarrhoea. On inspection the external genitalia were apparently normal. There was no evidence of any orifice or a depression in the natal cleft. On closer examination the situation of the anal opening could be made out in the fossa navicularis (Fig. 1). No sphincteric mechanism could be elicited at this orifice.

On deep palpation of the normal site of the anus a pair of cord-like structures about an inch long could be noted. A lateral X-ray of the bony pelvis (Fig. 2) showed a short sacrum ending bluntly; there was no coccyx and the ischial spines were inconspicuous. X-ray after a barium enema indicated the anus opening into the vagina. (Note the long rod in the vagina and the short one pointing to where the anus should have been (Fig. 3).) Since the patient and her husband could not be convinced of the harmlessness of this abnormality an attempt at operative correction had to be undertaken.

The patient was prepared as for any rectal surgery. On 19th September, 1960, the corrective operation was undertaken under spinal anaesthesia. Figure 4 shows the dilated anal orifice with the patient in the lithotomy position. A midline incision of about 4 inches long was made extending from the posterior margin of the anal opening extending towards the tip of the sacrum. Anteriorly the incision was carried around the anal margin in the lower part of the vagina. This was deepened to about an inch and a half by sharp dissection in order to isolate the anal canal. Figure 5 shows the extent of the dissection, and the anal tube directed towards its new position posteriorly. The perineal body was then built up by tiers of 2/0 chromic catgut sutures. Posteriorly the raw area was closed. The margins of the anal orifice were then sutured to the skin around with interrupted black linen. The final appearance with a dilator placed in the new anal canal is shown in Figure 6. A drainage tube in the anal canal was not considered necessary.

Post-operatively the patient was given mineral oil from the second night onwards. She had a spontaneous bowel action on the 5th day. On inspection on the 9th day the wound looked sound except that the mucous membrane of the anus was found to have retracted slightly inwards. There was some induration and discharge from the vaginal end. From then she continued to move her bowels at will. A regular rectal examination made on the 20th day showed the operated area to be well consolidated with no evidence of infection. The skin around the new anus manifested the cogwheel rugae typical of a normal anal margin, which the patient could contract (Fig. 7) and relax (Fig. 8) at will.

## Comments

Vestibular anus as a designation is as good as any for the condition referred to so long as it is realized that such an abnormal communication from the rectum opening anywhere on the posterior vaginal wall or fourchette may persist due to the defective formation of the ano-rectal septum. The associated malformation of the bony pelvis which this case presented had been noted also by Gordon Millar and Black. Surgical interference may not be indicated in infancy if satisfactory bowel evacuation is possible. The largest series of surgical intervention has so far been reported by Santulli (1952) who had undertaken these corrective measures at various stages of infancy and childhood. A preliminary colostomy had to be performed by him in a woman aged 28 as there was an associated condition of megacolon. He also appears to have undertaken an operative procedure because of the fear of the patient's marriage breaking up.

The steps of the operation as presented in this case are simple and could be easily adopted by any practising gynaecologist. No serious post-operative complications were met with and the success was complete both anatomically, functionally and psychologically.

## Summary

(1) Two cases of vestibular anus are presented and the nomenclature justified.

FIG. 1

Anal orifice situated in the fossa navicularis.

FIG. 2

X-ray pelvis shows a short sacrum, absent coccyx and ischial spines.

FIG. 3

X-ray after barium enema shows the anus opening into the vagina.

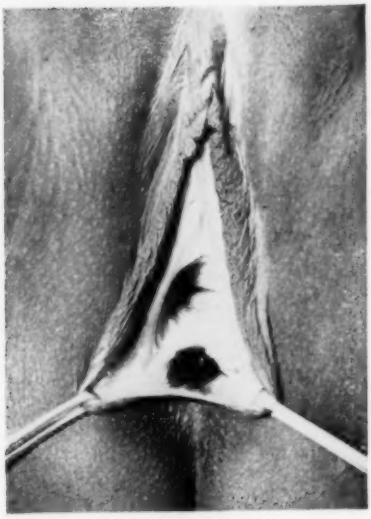

FIG. 4

Showing the dilated orifice under anaesthesia.

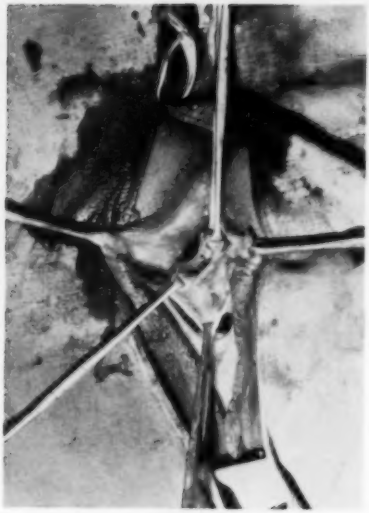

FIG. 5
Anal canal dissected and deviated to its new position posteriorly.

FIG. 6
The appearance of the anus.

FIG. 7
The surrounding skin showing the typical cogwheel appearance of the new anus when contracted.

FIG. 8
Anal sphincter relaxed.

P.M.N., S.K.

(2) One case was seen in labour at term and a lower segment Caesarean section was done. In the second case the anus was successfully re-positioned by surgical means.

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# A CASE OF GENITAL TUBERCULOSIS IN ASSOCIATION WITH PREGNANCY

BY

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GENITAL tuberculosis in the female usually leaves sterility in its wake. Nevertheless, medical literature contains a steadily growing number of cases in which pregnancy has occurred in association with genital tuberculosis of the mother.

In some of these cases the condition is known to have existed prior to pregnancy; in others the diagnosis is made after the pregnancy has terminated. In the second group it is seldom possible to say with certainty whether the condition existed before pregnancy or developed during it.

Most of the recorded cases are tubal pregnancies; the majority of uterine pregnancies end in abortion and seldom is pregnancy successful.

I record here a case of successful intrauterine pregnancy followed within a few weeks by symptoms due to genital tuberculosis.

The patient was a young Indian woman who had a pyrexia of unknown origin in the puerperium, following the delivery of a 31-weeks infant. About seven or eight weeks after delivery she began to experience "hot sweats" which caused her so much discomfort that she sought medical advice. She was admitted to hospital for investigation fourteen weeks after confinement. By this time the presence of a pelvic mass had been noted. Two weeks later the diagnosis of genital tuberculosis was confirmed by endometrial biopsy.

## CASE HISTORY

Mrs. V.P., aged 26, is a Hindu from the village of Pinsle in Bombay Province.

*26th October, 1958:* In apparently good health she arrived in the United Kingdom. She went straight to Wellingborough, Northamptonshire, and was married within a few days to a fellow countryman as previously arranged.

*15th November, 1958:* Last menstrual period. Fairly well during pregnancy; much troubled by sickness at first and later on complained of dyspnoea, a dry cough and several episodes of urinary infection. Seen very regularly by her own doctor—who had undertaken her confinement. Total weight gain during pregnancy was 6 pounds.

*16th June, 1959:* (31 weeks) Went into spontaneous labour. Promptly sent to a nearby maternity hospital which possesses a premature baby unit. She was delivered of a premature male infant weighing 2 pounds 14 ounces which survived. The baby's condition at birth was satisfactory considering its size. Examination of the placenta showed evidence of retroplacental bleeding before delivery: it was not examined histologically.

*17th June, 1959:* The mother's haemoglobin was 95 per cent and, owing to bed-shortage, the mother was transferred next day to the hospital in which confinement had been booked.

On admission to this latter hospital her temperature was 103° and her pulse rate 132. Appropriate routine investigations were instituted and a course of penicillin was started. The results of those investigations did not reveal a cause for the pyrexia.

*18th June, 1959:* Next day the patient's temperature was normal and remained so during

her stay in hospital with one exception; on the evening of the fifth day her temperature was 99° with a pulse rate of 84.

During her stay in hospital she complained of abdominal pain: she spoke no English and it was not found possible to elicit accurate information from her.

*3rd August, 1959:* Baby discharged home from hospital. It was bottle fed and weighed 5 pounds 5½ ounces.

*16th August, 1959* (8 weeks 5 days after delivery): Seen by family doctor: no details of postnatal examination.

*14th September, 1959* (12 weeks 6 days after delivery): Patient's husband requested doctor to see her as she had been having severe sweating bouts for several weeks. This apparently was her only complaint. Her temperature was 104° however and a lower abdominal mass was noted.

*19th September, 1959* (13 weeks 4 days after delivery): X-ray chest—negative.

*22nd September, 1959* (14 weeks after delivery): Admitted to local hospital for investigation: seen by a gynaecologist who confirmed the presence of large subumbilical tumour, apparently rising from the pelvis. The tumour was not tender and was smooth in outline.

*Investigations*

*23rd September, 1959:* Haemoglobin, 64 per cent, 9·4 g. Red blood cells, 4,410,000 per c.mm. White blood cells, 1,600/c.mm. (neutrophils, 64 per cent; lymphocytes, 34 per cent). Erythrocyte sedimentation rate, 41 mm. in one hour (corrected for packed cell volume of 33 per cent to 18 mm.). Sputum, nothing abnormal detected. No acid-fast bacilli culture—nothing abnormal detected. Urine, nothing abnormal detected. Culture, nothing abnormal detected.

Agglutination tests for *Salmonella typhi H, S. typhi O, S. paratyphi AH, BH* and *BO*, non-specific salmonellae, and *Brucella abortus*, were all negative.

*27th September, 1959* (14 weeks 3 days after delivery): Paul Bunnell—negative. X-ray chest—negative. Blood culture—negative. Mantoux—1 : 10,000, negative. Examination of faeces—negative. Culture—negative.

*28th September, 1959* (14 weeks 4 days after delivery): White blood cells, 5,000/c.mm. (neutrophils, 77 per cent; lymphocytes, 16 per cent; monocytes, 5 per cent; eosinophils, 2 per cent). Erythrocyte sedimentation rate, 52 mm. in 1 hour (corrected for packed cell volume of 35 per cent to 30 mm.).

*29th September, 1959:* Mantoux 1 : 1,000 slight positive.

*1st October, 1959:* Mantoux 1 : 100 positive.

During her stay in hospital the patient's condition progressively deteriorated. She lost weight, looked ill and ran a swinging temperature: this pyrexia was most marked usually in the evening when it frequently reached 102° F.

At this stage the diagnosis was still indefinite: tuberculosis was suspected. It was decided to perform an endometrial biopsy in the hope that this would shed further light on the problem.

*6th October, 1959:* Under cover of streptomycin and P.A.S. an examination under general anaesthesia was made.

A soft, fairly mobile pelvic tumour the size of a melon was made out: it appeared to rise from the right appendage. The uterus was rather bulky.

A gentle endometrial biopsy produced profuse, irregular curettings. Histological report on these curettings showed "tuberculous endometritis".

*13th October, 1959:* Transferred to sanatorium: streptomycin and P.A.S. continued.

*19th October, 1959:* Patient's condition much improved: no pyrexia: mass shrinking.

*20th October, 1959* (18 weeks after delivery): Mantoux test on baby, 1 : 1,000—positive. The baby's condition was good and it was thriving. There was some enlargement of the right cervical glands. Chest X-ray was negative.

## Pregnancy and Genital Tuberculosis

Reviewing 65,943 admissions to the Royal Samaritan Hospital for Women in Glasgow, Sutherland (1952) found 369 cases of genital tuberculosis (0·58 per cent).

Forty-seven of these were parous. In 5 cases out of the 47 the symptoms dated from pregnancy.

There is little doubt that the depressing effect of genital tuberculosis upon fertility is due to the damage it inflicts upon the Fallopian tubes. Yet Sharman (1958) found in his investigations of cases of genital tuberculosis that one-third of such cases had patent tubes. Presumably the vital activity of the tubal cells is impaired.

### The Use of Modern Drugs to Combat Tuberculosis

Generally speaking, surgery has failed to improve fertility prospects in those who suffer from genital tuberculosis. Modern drugs used to control tuberculosis offer more hope. Although the number is still small, several successful cases of pregnancy following genital tuberculosis have been published. Unfortunately there has been a more dramatic increase in cases of tubal pregnancy.

As Mills (1958) pointed out, for every successful pregnancy thus produced, a heavy toll of ectopics must be levied.

### Some Comments on Case Under Review

In the case of Mrs. V.P., it seems likely that infection occurred either immediately prior to pregnancy, or in the very early stages.

She arrived in Britain in apparently good health on 26th October, 1958 and was married within a few days.

On 15th November, 1958 her last menstrual period occurred.

On 16th June, 1959 she was delivered of a live 31-weeks infant.

On 14th September, 1959, less than 13 weeks after delivery, she was found to have an abdominal mass: at that time she was complaining of "hot sweats" of several weeks duration.

In recent years the town of Wellingborough, Northamptonshire, has shared with other areas of industrial Britain in the influx of foreign workers. It now has quite a large Indian community.

Impressed by the high incidence of pulmonary tuberculosis which seemed to develop after arrival among the Indians in Wellingborough, Dr. Corbett—who is Mrs. V.P.'s family doctor, began to X-ray each one on his list as the opportunity presented itself. Out of 22 Indians on his list at the time of writing, 10 have developed tuberculosis: in every case the initial chest X-ray was negative and so it seems likely that the infection developed after arrival in Wellingborough.

Unfortunately Mrs. V.P. was not X-rayed on arrival—but it seems likely that, in common with her countrymen, she was free of tuberculous infection on arrival and that the infection developed subsequently.

### Summary

(1) A case of genital tuberculosis in association with successful pregnancy is described in a young Indian woman.

(2) Abdominal masses were felt 12 weeks 6 days after delivery and at that time she had complained of hot sweats for several weeks.

(3) Evidence is produced which suggests that infection occurred either immediately before pregnancy or in the early stages.

(4) Attention is drawn to the difficulties in diagnosis in such a case. Genital tuberculosis is so rarely seen in association with pregnancy that in the first instance it is difficult to avoid a bias against this diagnosis.

(5) The baby had a Mantoux Test positive 1 : 1,000, 18 weeks after delivery. Unfortunately the placenta was not examined histologically.

(6) Attention is drawn to the high incidence of tuberculosis occurring in immigrant Indians in an English industrial town.

I wish to thank Mr. R. J. Watson, F.R.C.S.(Ed.), F.R.C.O.G., and Miss S. Lehane, M.R.C.O.G., for permission to publish this case. I also wish to thank Dr. Corbett of Wellingborough.

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# ADENOMATOSIS VAGINAE

BY

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VAGINAL adenomatosis is a rare condition. When Bonney and Glendining first described a case in 1910 their paper was entitled "Adenomatosis Vaginae; a hitherto undescribed condition". I have been able to find only three cases that fit the original description since then. Three cases are here reported and in one of them the extraordinary event had occurred of spread on to the vulva. Case 1 was under the care of Professor Harvey Evers, Case 2 under Professor J. K. Russell and Case 3 was under my own care but all of them were seen and examined by me. I am indebted to these gentlemen for permission to include their cases in this paper. The condition is one of replacement of the normal squamous epithelial covering of the vagina by a columnar gland-bearing epithelium. Mucus-secretion is active and the presenting symptom is a profuse discharge of clear mucus, like white of egg. The aetiology is unknown and an effective treatment is unknown. The pathology and clinical appearances will become evident in the description of the histories of the three patients.

*Case 1.* Mrs. E.C., aged 37, was first admitted to the Royal Victoria Infirmary in December, 1957 with a complaint of a profuse, non-irritant vaginal discharge for nine years. She needed to wear a diaper persistently. There were no other relevant complaints and she did not complain of dyspareunia. She had first been seen with this complaint as an out-patient in 1950 but had been lost sight of due to changes of address. Speculum examination at that time had not shown anything abnormal except some excess of mucus from a normal looking cervix. The discharge had begun to trouble her four years after the birth of her first child in 1945. This had been a normal confinement as were her two others in 1950 and 1952. There was a history of rarely occurring attacks of asthma for six years. Menstruation was rather heavy but regular 5/26.

On examination she was a fat woman with no important abnormalities except in the genital system. Haemoglobin 86 per cent; weight 14 stones. Examination under an anaesthetic (Dr. Peter Mitchell) showed the whole of the anterior vaginal wall and the upper three-quarters of the posterior wall, dark red in colour and stippled with granular cysts from pin prick to pin head size (Fig. 1). There were a few cysts up to 5 mm. in diameter. There was a well-marked line of demarcation from the remaining normal vaginal covering and from the portio vaginalis cervicis which was normal except for a small circumoral erosion. Clear mucus was pouring out of the vaginal orifice. The vagina was not constricted. The other pelvic organs felt normal. Specimens for biopsy were taken and curettage performed. I have to thank Dr. R. O. K. Schade for the descriptions of the pathology.

"There are two fragments of tissue from the vaginal wall. Histologically one fragment shows complete loss of squamous epithelium (Fig. 2) and the other shows the junction of apparently normal vaginal wall with a gland-bearing portion (Fig. 4). The gland-bearing portion has its surface denuded of any epithelium and shows, just below the surface, closely packed glands similar in structure to those seen in the cervix. Some of these glands open on the surface but others are dilated and form small cysts. The

stroma in which the glands are embedded is oedematous and shows minimal inflammatory changes (Fig. 3). The endometrium is in the proliferative stage with a somewhat oedematous stroma."

Two months later further specimens of the vaginal wall were taken and submitted to bacteriological culture. *Bacillus proteus*, *Staphylococcus albus*, pneumococci and anthracoid organisms were grown but it was not thought that any of these had aetiological significance. Pessaries containing 10 mg. of methyl testosterone were prescribed and she inserted one nightly for seven weeks. The symptoms and the state of the vagina remained quite unaltered.

*Case 2.* Mildred N., aged 34, was first admitted to the Royal Victoria Infirmary in February, 1956. She had been seen as an out-patient in 1952 complaining of dyspareunia and a diagnosis of "tight vaginal introitus" had then been made. She did not come in when sent for. Her history is so full of incident that I put it in résumé form:

1923 March. Date of birth.

1934 Rheumatic fever. She has since had a well-compensated mitral stenosis.

1942 Married first husband.
Three months miscarriage.

1951 Princess Mary Maternity Hospital. Birth of macerated baby weighing 4 pounds at 38 weeks. No cause for foetal death found. No abnormality noted in vagina at postnatal examination.

1952 Seen as an out-patient for dyspareunia.

1955 Married second husband.
Three months miscarriage. Curetted at another hospital.

1956 February. Admitted Royal Victoria Infirmary complaining of continued dyspareunia and discharge. Biopsy of the vaginal wall established the nature of the condition.
June. Second biopsy and bacteriological examination.
September. Princess Mary Maternity Hospital. Admitted for threatened miscarriage at 9 weeks.

1957 March. Princess Mary Maternity Hospital. Caesarean section on account of obstetric history and the state of the vagina. Healthy child weighing 5½ pounds.

1958 Royal Victoria Infirmary. Third biopsy and photograph.

1961. January. Caesarean section and tubal ligation. Healthy child weighing 6½ pounds.

Her complaint throughout has been of constant pain in the vagina and of introital dyspareunia. She is constantly wet from a profuse discharge of thin mucus. There are several detailed descriptions in the notes (including one of my own) with expressions such as "red raw", "acutely inflamed vagina" and "large granulating areas" but the clearest description is that of Professor J. K. Russell in January, 1958:

"There is a copious discharge of clear mucus. The anterior vaginal wall is red and granulomatous with some small vesicles scattered round the edges. The whole anterior vaginal wall is affected but the cervix is normal. The posterior vaginal wall is affected to within ¾ inch of the introitus and shows a sharp line of demarcation from the remaining normal vaginal covering. The whole of the affected vaginal wall is thickened and rigid."

Biopsy specimens were reported:

"Endometrial scrapings and two small pieces of vaginal wall. Both the fragments of vaginal wall are entirely denuded of squamous epithelium. On the surface lies an eosinophilic material containing scanty inflammatory cells (Fig. 5) but in parts a single layer of cuboidal epithelium appears to cover the surface (Fig. 6). As in the previous case numerous partly cystic glands can be seen, many of them opening on to the surface. The stroma in which they are embedded shows oedema and in some areas well marked chronic inflammatory changes. The endometrium is normal in the proliferative phase."

Bacteriological examination of the piece of vaginal wall showed no organisms and none was grown on various media including those for *Mycobacterium tuberculosis*.

FIG. 1

Case 1. This shows the junction of the adenomatous area with the normal skin on the posterior wall of the vagina.

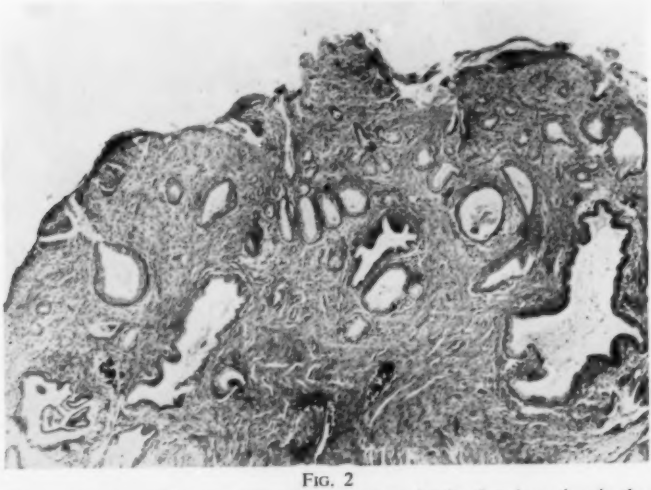

FIG. 2

Case 1. Vaginal wall. Low power view to show glands of various sizes in the corium.

F.S.

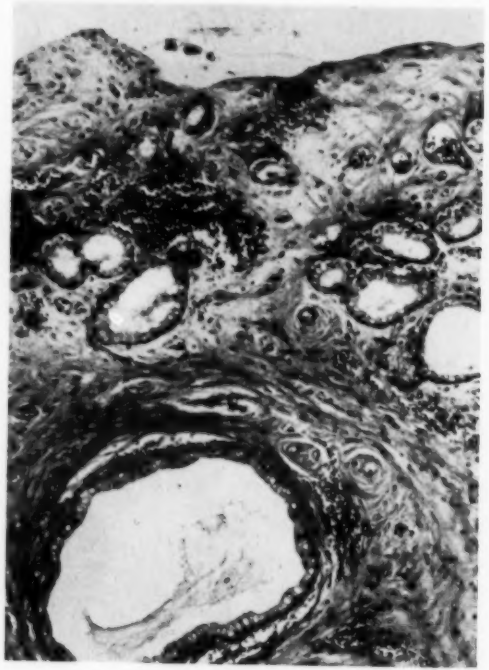

FIG. 3

Case 1. Vaginal wall. In some areas there is inflammatory reaction and oedema amongst the glands.

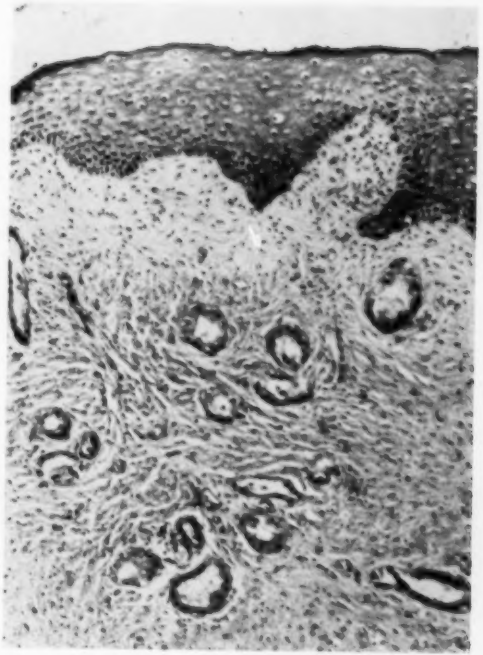

FIG. 4

Case 1. Vaginal wall. At the edge of the affected area the adenomatous process extends under the normal vaginal skin.

FIG. 5
Case 2. Vaginal wall. In this patient there was much coagulated mucus on the surface.

FIG. 6
Case 2. Vaginal wall. This was the only place at which a surface covering was seen—a single layer of low epithelial cells.

F.S.

FIG. 7
Case 3. Adenomatosis vaginae involving the vulva.

FIG. 8

Case 3. Vulva. The end of the normal skin is seen on the left and the beginning of the adenomatous area on the right. The intervening tissue has no epithelial covering.

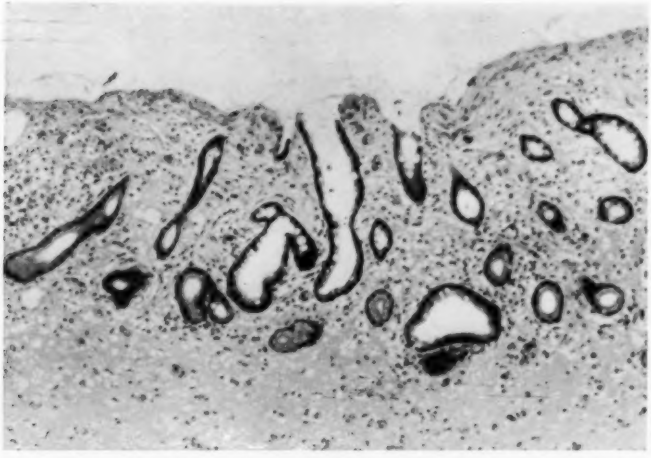

FIG. 9

Case 3. Vulva. Glands very like those of the cervix are opening on to the denuded surface of the vulva.

*Case 3.* Mrs. D.T., aged 52, was admitted to the Royal Victoria Infirmary on 5th January, 1960, with a diagnosis of "incontinence of urine" since the birth of her only child in 1937. To leading questions she replied that there had been a troublesome excess of mucus even before this and before marriage. She said that the delivery was by instruments and had been followed by "septic vagina and white leg" for which she was kept in hospital for six weeks. Menstruation had been normal until the menopause twelve months before admission. There was no history of any important illness. She had had pruritus vulvae for as long as the discharge had been present and had had one or two attacks of dysuria and frequency of micturition. She had some chronic bronchitis but otherwise her general health was good.

On examination the anterior part of the vulva in front of the root of the clitoris and on to the mons veneris showed the ordinary lichenified changes from scratching. Quantities of thin clear mucus were pouring out of the vulval introitus. Around the introitus and on each side involving the remnants of the atrophied labia minora were stippled smooth red areas with clear-cut margins (Fig. 7). Inside the vagina, which was rigid and somewhat narrowed the walls were granular, purple, shining and markedly engorged. The whole of the vaginal walls had a surface like that of a mucous polyp of the cervix. The cervix felt scarred but otherwise normal. It was not seen due to the constriction of the vagina. The rest of the pelvis felt normal. There was no abnormality in the buccal mucous membrane or elsewhere as in Behçet's syndrome. Biopsy specimens were taken from inside the vagina and from the edge of the vulval lesion to include the adjacent skin.

"A fragment from the vulva, fragment from the vagina and uterine curettings. Histologically the vulval fragment is covered partly by squamous epithelium but in other parts the squamous epithelium is completely lost. The squamous epithelium present shows a mild degree of hyperkeratosis and is rather atrophic. It has lost its papillary structure. Just deep to it one finds a band-like layer of fairly dense chronic inflammatory infiltration. The underlying tissue is oedematous and intensely congested. In the parts of the vulval surface denuded of squamous epithelium there is a small amount of chronic inflammatory change (Fig. 8). Here one sees numerous mucus-secreting glands lying within a highly oedematous connective tissue stroma (Fig. 9). Some of the glands can be seen to open on the surface. The type of the glands corresponds with those seen normally in the cervical canal.

"The fragment of vaginal wall examined is entirely denuded of squamous epithelium. Deep to this denuded surface and opening on to it are closely set glands of the same type as described in the section of vulva. Chronic inflammatory reaction is marked in small areas and the deeper layers of the vaginal wall are oedematous.

"The uterine curettings show normal endometrium apparently in the proliferative phase."

One per cent hydrocortisone cream was prescribed for the lichenified areas adjacent to the adenomatous lesion and two months later she stated that she was relieved of the irritation and pruritus. The outpouring of mucus has continued and the condition inside the vagina and on the vulva has not changed.

This patient is now (December, 1960) making a good recovery under chemotherapy from a small area of pulmonary tuberculosis. An opportunity has been taken of measuring her output of vaginal mucus in twenty-four hours. A total of 16 grammes was produced but one's clinical impression is that the two other patients had a more profuse production of mucus.

## Discussion

In each of the three patients there was a very profuse discharge of clear mucus. In none of them was the discharge purulent but in Cases 2 and 3 there was rigidity of the vaginal walls from inflammatory reaction and scar tissue deposition. In none of them did symptoms sufficient to need medical attention arise until she had had a pregnancy. In Case 1 the cells lining the glands were high columnar whereas in Case 2 they were cuboidal and in Case 3 intermediate. Case 1 appeared to secrete the greatest amount of mucus. The sole symptom in Case 1 was the constant wetness from the discharge. In Case 2

there was dyspareunia from the rigidity of the vagina and tenderness of the raw surface. Her discharge was sufficient for her and her doctor to think that she had incontinence of urine. Case 3 had pruritus but this was around the clitoris and mons which were sore from scratching. This cleared with hydrocortisone cream leaving the adenomatous area unaffected.

It seems incredible that uncovered dermis could be present over a period of years without the production of a purulent discharge. Inflammatory changes were present in two of the patients but one showed very little inflammatory reaction. One can only suppose that by being constantly bathed in mucus the areas were kept protected from florid infective processes.

We have not been able to find a treatment that has any effect on the condition. It seems unlikely that removal of any of the pelvic organs would make much difference when, as in Case 3, the condition can persist after the menopause.

The case reported in 1910 by Bonney and Glendining appears to be similar to those now reported. Bonney and Glendining quoted a paper by von Preuschen in 1877 describing a condition in which some mucous glands opened on the vaginal surface but there was no mention of hyperplasia of the glands and no clinical description. Plaut and Dreyfuss (1940) wrote a comprehensive article on Adenosis of the Vagina including a review of published cases. It would seem likely that different conditions are included in their survey. They fall into three groups. There are cases in which by search pathologists have found a few symptomless patches of gland tissue sometimes dilated to form cysts, under the vaginal epithelium. To this group would belong the accounts of Davidsohn (1900), Poupinel (1889), Whitehouse (1922) and one of the three cases of Plaut and Dreyfuss. In other cases there is a localized sub-epithelial adenoma, perhaps ulcerated on its surface and situated in the upper part of the vagina (Spencer, 1923; Schiller, 1924; and one of Plaut and Dreyfuss' patients). The only cases that appear to fit with the clinical and pathological condition now described are those of Bonney and Glendining, Haultain (1911), Scannell (1939), one of Plaut's cases (originally described in 1927) and possibly that of Meyer (1903). In this last group of cases the process appears to have been diffuse and spreading slowly.

All those who have recorded cases have inclined to the opinion that the condition was either the result of differentiation of originally indifferent Müllerian vaginal cells or of metaplasia of cells of Müllerian origin. All write of Müllerian embryonal cells developing into gland tissue. This could account for the first two groups where gland tissue is found in the upper part of the vagina either quiescent under the surface epithelium or forming cysts or a localized adenoma. This would not account, however, for the diffuse type and certainly not for the case here described in which the process had spread on to the vulva. The appearances are exactly those of a cervical erosion and the inclination of modern opinion is to regard this as due to hormone activity. I would suggest as a possibility worthy of further investigation that these conditions might be due to the *local* action of hormones from the ovary—that the hormones in excess or in degraded form, traverse the Fallopian tubes and the uterus and pour over the epithelium of the cervix. If they have not been utilized or absorbed by the endometrium or by the cervical glands they may be able to induce metaplasia in the vagina or even on the vulva. The ability of ovarian hormones directly applied to a surface to produce metaplasia and hyperplasia might even be extended to include such conditions as endometriosis and metropathia. The condition reported here might well be designated vaginal endocervicosis.

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# ECTOPIC PREGNANCY FOLLOWING HYSTERECTOMY

BY

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MRS. A.E.J., aged 41, para-3, had her last pregnancy terminated by Caesarean section in 1955.

On 28th April, 1960, I performed a hysterectomy on account of metropathia. Both ovaries were healthy and were preserved. Recovery was uneventful and she returned home on the 12th day after the operation.

On 24th May, 1960, she complained of sudden pain in the left iliac fossa and was seen by one of my colleagues, Mr. S. Loxton, who considered that the pain was large bowel in origin and warned a surgical colleague that he might be asked to see the patient. The symptoms, however, subsided, and he was not asked to see the patient.

On 6th June, 1960, she complained of a sudden severe pain in the left iliac fossa and fainted. The history was typical of a ruptured tubal pregnancy but this was discounted by me as hysterectomy had been performed previously.

On abdominal examination there was tenderness in the lower abdomen and some large bowel distension. On vaginal examination no mass was palpable in the pelvis. The patient's general condition was good.

On 7th June, 1960, the abdomen was obviously more distended though no free fluid could be detected.

I asked a surgical colleague, Mr. Bartlett, to see the patient with me and he advised laparotomy. Haemoglobin was down to 55 per cent and so blood transfusion was commenced and later laparotomy was performed.

On opening the abdomen there was free blood in the pelvis and a mass was found in the ampullary portion of the left tube which was an obvious ectopic pregnancy. The tube was removed and the abdomen closed, and the patient made a rapid recovery.

The history in summary was as follows. Her last menstrual period was from 9th to 14th April and therefore ovulation occurred between 19th and 24th April. Hysterectomy was performed on 28th April. Coitus had taken place on 25th April and no contraceptive had been used. Previous to this date a contraceptive had been used regularly.

It would appear, therefore, that at operation the left tube contained a fertilized ovum and, as the tube had not been removed at operation, the pregnancy continued and, of necessity, remaining *in situ*. The ectopic pregnancy was of the tubal abortion type, giving its first warning of trying to abort on the 26th day following hysterectomy, and its final attempt on the 40th day.

I have reported this case as I have never seen or heard of such a case previously. Ectopic pregnancies have occurred after hysterectomy, but in these cases there must have been a patent cervical canal, or a sinus into the peritoneal cavity from the vaginal vault.

# BEHAVIOUR PATTERNS IN LABOUR

## A Study of 776 Consecutive Patients

BY

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> "There is no more effective medicine than kindness nor is there any substitute for it. It is an essential ingredient in all human relationships when one is frightened and lonely." *Rardin*, 1960

IN this country today antenatal care is the rule rather than the exception and the dangers of childbirth have, in consequence, been greatly reduced. It is inevitable, therefore, that greater consideration of the mother's feelings during childbirth should be the next step forward in this natural progression. Before the question of "Human Relations" had become a popular subject for both the profession and the public, a survey was made of the reactions of 776 consecutive maternity cases at the West Middlesex and Chiswick Maternity Hospitals.

The Government White Paper (Ministry of Health, 1961) rightly stressed the importance of overcrowding, understaffing, and unsuitable accommodation. Yet the popular Press gave little space to these factors, emphasizing mainly the lack of tolerance and understanding by hospital staff, thereby provoking a public outcry which soon reached alarming proportions.

Whilst recognizing the need for improvement, it is important to remember that this aspect of the White Paper was based only on patients' complaints. Mothers who complain are a selected minority and cannot, therefore, represent the views of the average British woman in childbirth. Indeed, in the course of one year in the above hospitals, the only two complaints made directly to Government officials originated from a foreign subject and a patient whose paranoid delusions had at one time required institutional treatment. Based on the annual birth rate, 500 complaints from similar subjects might be received in the course of one year throughout the whole country. This example serves to illustrate the need for some controlled consideration of the subject.

Professor Norman Morris (1960), whose work aroused interest in the emotional management of childbirth, dealt with many aspects of the subject from the first antenatal visit to the end of the lying-in period. This present enquiry concerns the narrower field of labour, antenatal factors being included only if they were thought to have a bearing on the patients' ultimate behaviour in labour. It would be difficult not to recognize the truth of the remarks in the many letters quoted by Professor Morris; however, the fact that these letters were mostly well written and described graphically the points of discord, suggested that they came from a literate and possibly well-educated section of the community. Though their remarks are important, they represent a selected group. In order to include those women who were either unable or disinclined to write letters, every patient in this series was given pen and paper and invited to write down her criticisms and complaints. Facilities for dictation were afforded to those patients who were unable to read or write.

This series included every case in labour between October and December, 1960, whether emergency admission or booked case. Two questionnaires were used to assess results: the first was completed by the midwife in charge and the second by the patient shortly after delivery, before she could be influenced by the

remarks of other mothers. Approximately half these patients were given a second, identical questionnaire on the sixth day, in order to compare their reactions just before going home with those immediately after delivery.

Apart from data concerning the labour, the midwives' questionnaires included an assessment of the patient's emotional state on admission and throughout labour. The patient's form required answers to a number of questions, indicated by a tick in the appropriate column. However, to avoid complete regimentation, several spaces were provided for free expression. These produced many valuable individual comments, which would otherwise have been omitted.

Before analyzing any figures, it is essential to give a picture of the unit and its staff, together with the nature and volume of the population it serves.

There are 165 maternity beds, divided into 38 antenatal, 107 lying-in and 20 associated with the management of labour. Eleven single rooms are available for antenatal and ten for postnatal cases. Labour is conducted in three separate units, with a total of 9 labour wards, 4 receiving wards, and 8 first-stage beds. There is no single ward or sitting-room accommodation for patients in the first stage, nor are there waiting rooms or toilet facilities for husbands or other visitors. These features alone would make it impossible to implement the recommendations of the White Paper.

The unit is staffed by 4 consultant obstetricians and 14 doctors below that rank. Approximately 78 qualified midwives and 60 pupils are employed at any one time, to cover work in the Antenatal Clinic and maternity wards. For maternity cases, the hospitals serve a population of about 400,000 living in well-populated outer London suburban districts. The majority of patients come from Social Classes 3 and 4, and surprisingly few immigrants have settled in the area, despite the very high proportion in neighbouring districts.

Approximately 70 per cent of cases referred to the Booking Clinics are accepted, though this frequently involves overcrowding, or early discharge from hospital, the average duration of the lying-in period being 8 days.

Selection of cases is made on medical and social grounds. The former are determined by the following categories:

(1) Primigravid patients aged over 30 or under 18.
(2) Patients with a medical or obstetrical abnormality.
(3) Multiparous patients with a bad obstetric history.
(4) Multiparous patients who have had 4 or more children.

Bookings on social grounds were made by the almoners, representing approximately one-third of the total.

The following figures related to 1960:

| | |
|---|---|
| Total attendances at Booking Clinics | 4,409 |
| Total number of cases booked .. | 3,181 |
| Number of cases booked on medical grounds .. .. .. .. | 2,143 |
| Number of cases booked on social grounds .. .. .. .. | 1,038 |
| Number of primigravidae refused bookings .. .. .. .. | 503 |

Over the last five years, the average number of deliveries per year has been 3,302; approximately 8 per cent of these were emergency admissions.

In view of the size of the staff, patients attending the hospital throughout their pregnancy might see a different doctor and midwife on each occasion. This did not help to achieve the peace of mind and quiet confidence required at the onset of labour.

It can be seen from these preliminary observations that the stage-setting for this survey was not perfect. Neither the pressure of work nor the standard of accommodation allowed for an ideal communion between patient and midwife.

For the purpose of this survey, consecutive cases have been taken; only patients admitted for elective Caesarean section have been excluded.

### Type of Patient

England, Wales and Scotland provided 439 (56 per cent) of these patients. A further 191 (25 per cent) described themselves as "British", but it was not known what proportion of these

had obtained their nationality by naturalization. Ireland provided 74 (9 per cent); the rest of Europe 30 (4 per cent); and the remaining 42 (6 per cent) were divided between Africa, the West Indies, the Middle and Far East.

The patients' religions conformed to the expected pattern: 502 (65 per cent) claimed allegiance to the Church of England and 179 (23 per cent) were Roman Catholics; 47 (6 per cent) were Jewish and the remaining 48 (6 per cent) belonged to other faiths, or claimed no religion at all.

Assessment of marital status showed that 12 per cent of primigravid patients were single; however, on their own admission, a further 26 per cent were unmarried at the onset of their pregnancy. Among the multiparous patients, 1 per cent were unmarried at the time of delivery.

Parity distribution showed 408 primiparae and 368 multiparae; 87 per cent of their ages were between 20 and 35, leaving insufficient numbers to make an independent study of the younger and older age groups.

## Training for Labour

Much puolicity has been given to the behaviour of midwives towards their patients, but little attention has been paid to the part played by the patient herself, and her nearest relatives, in preparing for labour. In this country, many free facilities are available to the young expectant mother in the form of books, lectures and relaxation exercises, yet surprisingly few take advantage of them. It is interesting to consider these means of education in greater detail.

### (a) *The Written Word*

It is perhaps too sweeping to use the title "Books", as much of the information is supplied in pamphlet form or as incidental observations in books on other subjects.

In the past, when literature was scarce and printing expensive, the only source of information was the Bible, which provided an answer to most problems of social behaviour. It must therefore have fashioned the woman's approach to childbirth for many generations. However, it contains little but cold comfort for the young pregnant woman seeking advice. In the early chapters she discovers that all women must suffer for the transgressions of Eve, "I will greatly multiply thy sorrow and thy conception; in sorrow thou shalt bring forth children." In order to emphasize this prediction, subsequent references to childbirth mostly concern painful abnormalities of labour. Indeed, the mothers died in two of the three instances where labour was described in detail.

During the last thirty years, many books and papers have been written to suit all grades of intelligence. Read (1933) pioneered the subject of Painless Childbirth. The strength of his personality must have been hypnotic and, indeed, much of his success was probably due to hypnosis. However, his convictions expressed in writing have not always proved as helpful to the patient as his presence in the labour room. In 1949 he stated, "Pain is an emotional anomaly and the cause of pain in uncomplicated labour is fear. Fear of childbirth is an artefact to which society has justifiably succumbed. For medical science has accepted pain as an essential accompaniment to parturition." This sweeping over-simplification of a complex subject typifies his unbending style of presentation. Among the patients of lesser mortals, pain still presents the greatest single problem even when all Read's advice has been carefully followed; this was true for the majority of patients in this series. Read (1933) had this to say about these patients who failed to achieve painless childbirth, "Failure is due to the mentality among modern, cultured women where no influence can bend the rigid egoism of their labour."

Dogmatic teaching, whether in support of painful or painless labour, is certainly harmful to some sections of the community. Teaching must apply to that great majority of patients who may not be fortunate enough to have a personal doctor or midwife in attendance. To these, a simple explanation of the nature and control of labour pains would be more valuable than an insistence that the presence of pain is an indication of failure.

It is perhaps surprising that, despite the wealth of literature available today, only 57 per cent of primiparous patients had read anything

concerning childbirth by the time their baby was born.

(b) *The Spoken Word*

Lectures on childbirth were freely available to all mothers, yet only 27 per cent of primigravidae attended them. It is therefore apparent that most of their instruction took place in their homes or among their immediate friends.

The scope of the enquiry was too limited to study the help given to the young primigravidae by women in her home environment who had borne children themselves. However, it was possible to determine the number of patients who had been frightened by thoughtless gossip about childbirth. Each mother was asked if any friends or relations had told her dreadful stories of their confinements. Of 408 primiparous patients, 132 (33 per cent) had been exposed to such obstetric reminiscences, no doubt exaggerated by time and telling.

At this point, it is interesting to note that many writers and women's societies have advocated that midwives should be replaced by this group of experienced mothers. Their argument is largely based on the assumption that the nulliparous midwife is psychologically unsuitable and faced with various frustrations associated with her childless state.

This may sometimes be true, and, as the midwife is constantly in the public eye, any evidence of this tendency will immediately be publicized. The alternative group of parous women who surround the young expectant mother in her home environment is better protected and consequently less open to criticism than the midwives. Their suitability as attendants in labour can, therefore, only be based on the fact that they have experienced childbirth themselves. However, many of them are apparently unable to resist the temptation of relating their own unpleasant experiences, which, with no scientific training, they may assume are normal occurrences in labour. Thus, their parity alone may be sufficient reason to keep them away from the young patient in labour. However, 67 per cent of patients were not submitted to these stories and it is probable that this group found comfort and encouragement in their home surroundings.

(c) *Antenatal Exercises*

Antenatal exercises were considered beneficial several centuries before the birth of Christ, though the woman of today would hardly submit herself to the athletic contortions recommended at that time. Burnett (1956) in a review of 2,675 cases delivered in the same hospitals as the patients of this series, showed that relaxation exercises in no way altered the course of labour, nor did they reduce the complications. It was therefore somewhat doubtful whether they served any useful purpose. However, whilst considering fear and pain in a later paragraph of this paper, it was shown that, though the perception of pain appears to be unaltered, the degree of fear is reduced in patients who attended relaxation classes. Their value may therefore be in the psychological rather than the physical preparation for labour.

In 1956, Burnett found that 18 per cent of primiparous patients attended these classes; this figure had risen to 35 per cent in the present series.

## The Attendance of Husbands and Other Relatives During Labour

The functions of a husband in relation to his labouring wife have never been clearly defined though they have recently become the subject of much controversy.

In many primitive races, the husbands associate themselves with childbirth by means of a Couvade. This was thought to be an attempt to share or reduce the woman's suffering during labour. However, a more cynical opinion suggested that it was the father's attempt to associate himself with his unborn son, and thereby emphasize the bond of blood between them. As he had no preternatural knowledge of the child's sex, he was obliged to give a good performance on each occasion.

Clark (1956) described the Couvade among the Campa, one of the most primitive races left in existence, living in the Amazonian jungle. He wrote, "The true reason the Campa husband retires to his bed in pain is because he believes he is lessening his wife's suffering in so doing. He believes he is bearing her pain for her. And she believes it too, believes it with all the vivid

and sometimes terrible conviction of the Campa mind. As a result, the wife works at hard labour up to the hour of birth and then again within a few hours of having her baby . . . therefore the husband is not necessarily stealing the wife's thunder in order to receive attention from his condoling friends and to get their gifts, as is generally believed." Whatever the motive for the Couvade, it is apparent that the husband suffered, but never in the company of the wife. Can any similarity be found in the approach of husbands in a more civilized world?

Diametrically opposed views are held, both by members of the public and the medical profession, on the question of a husband's position in relation to his wife in labour. Some measure of agreement has been reached over the first stage, as the husband can often be of value in supporting and comforting his wife. However, the delivery presents a different problem. Many complex psychological reasons have been given in support of his presence, but it is possible that the underlying motive is usually curiosity. This motive has been described as unnatural curiosity. This is certainly not accurate, for what could be more natural than a man's attempt to penetrate the barriers of reticence which have surrounded this essentially feminine process for many generations? Even though the curiosity is natural it is hardly an acceptable reason for allowing the husband to be present during the delivery. Davis (1961) suggests that the reason may be sadistic curiosity, and that the husband's presence will embarrass and hinder the medical attendant, and may even be fraught with danger and disillusionment to the husband himself. On the other hand, many people have written in favour of their presence during delivery. Hill (1961) suggests that it is the creative climax of the physical relationship. He finds support from Burne (1961), who goes further by warning of the possible guilt complexes and paternal frustrations which may follow exclusion from the labour-room.

Before theorizing about the rightful place of the husband, it seemed advisable to study the views of each partner in relation to this problem. Four questions on this aspect were asked, and

TABLE I

*The Presence of Husbands During Labour*

| | Wives | | | Husbands | | |
|---|---|---|---|---|---|---|
| | Primi-parae | Multi-parae | Total | Primi-parae | Multi-parae | Total |
| In favour of husband's presence only during the first stage .. .. .. | 134 | 112 | 246 (34%) | 92 | 65 | 157 (22%) |
| In favour of husband's presence only during the delivery .. .. .. | 34 | 32 | 66 (9%) | 36 | 36 | 72 (10%) |
| In favour of husband's presence during first stage and delivery .. .. | 33 | 28 | 61 (8%) | 45 | 43 | 88 (12%) |
| Not in favour of husband's presence at any time during labour .. .. | 167 | 184 | 351 (48%) | 191 | 203 | 394 (53%) |
| Did not know .. .. .. .. | 5 | 4 | 9 (1%) | 9 | 13 | 22 (3%) |
| Total .. .. .. .. .. | 373 (51%) | 360 (49%) | 733 (100%) | 373 (51%) | 360 (49%) | 733 (100%) |

in half the cases they were repeated on the sixth day of the puerperium. Corrections were made for unmarried mothers and unanswered questionnaires.

The questions were as follows:

(1) Would you like your husband to be present during early labour?
(2) Would you like your husband to be present during delivery?
(3) Would your husband have liked to be present during early labour?
(4) Would your husband have liked to be present during birth of the baby?

Details are shown in Table I.

### Attendance at the Delivery

As the husband's presence at delivery is the most controversial subject, a further analysis was made, considering this factor alone. (Table II.)

These figures show a remarkable similarity between the views of primiparous and multiparous patients. Approximately half the mothers would prefer not to have their husbands in attendance at any time during labour; slightly more husbands shared this view. Very few wives wanted their husbands to be present throughout labour, indeed, the figure was only 8 per cent. Many more wanted him there for the first stage (42 per cent), but the husbands themselves were not quite so enthusiastic (35 per cent). Only 17 per cent of women would like their husbands to be present at the delivery, and 22 per cent of husbands would like to be there. In this small group of husbands, approximately 50 per cent wanted to watch the delivery without being present during the first stage; and 39 per cent wanted to do so without the approval of their wives. In 201 (27 per cent) cases, there was some disagreement between husband and wife, and in 25 per cent, husband or wife, or both partners had changed their minds by the sixth day of the puerperium.

Considering this question as a whole, there seems to be as much disagreement within the family itself as there is among the medical attendants. It is apparent that many women may be helped by the presence of their husbands in the first stage but the figures for the birth itself do not favour a determined effort to press for a change in our present approach. Indeed, it is surprising that so much has been written in support of so small a minority. The number of husbands who wanted to be present only at the delivery, and, in many cases, against the wishes of their wives, lent support to the opinion that the underlying motive is one of curiosity rather than the desire to support a labouring wife. In fact, if this is the climax of human relationship,

Table II

*The Delivery*

| | Wives | | | Husbands | | |
|---|---|---|---|---|---|---|
| | Primiparae | Multiparae | Total | Primiparae | Multiparae | Total |
| In favour of husband's presence during the delivery .. .. .. .. | 67 | 60 | 127 (17%) | 81 | 79 | 160 (21%) |
| Not in favour of husband's presence during the delivery .. .. .. | 301 | 296 | 597 (82%) | 283 | 268 | 551 (76%) |
| Did not know .. .. .. .. | 5 | 4 | 9 (1%) | 9 | 13 | 22 (3%) |
| Total .. .. .. .. .. | 373 (51%) | 360 (49%) | 733 (100%) | 373 (51%) | 360 (49%) | 733 (100%) |

TABLE III

*The Time of Maximum Distress*

| | Primiparae | Multiparae | Total |
|---|---|---|---|
| Soon after admission to hospital .. .. .. | 20 | 24 | 44 (6%) |
| Just before being moved to the labour ward .. | 149 | 107 | 256 (33%) |
| In the labour ward .. .. .. .. .. | 138 | 92 | 230 (30%) |
| During the delivery .. .. .. .. .. | 78 | 117 | 195 (25%) |
| After the delivery .. .. .. .. .. | 9 | 14 | 23 (3%) |
| Not answered .. .. .. .. .. | 14 | 14 | 28 (3%) |
| Total .. .. .. .. .. .. | 408 (53%) | 368 (47%) | 776 (100%) |

it is surprising that only one-fifth of the population wish to reach it.

It was considered likely that some women would prefer to have a close relative with them during labour. However, this was not borne out by investigation, as only 38 (5 per cent) expressed this wish. Of these cases, 24 were primiparous and 14 multiparous; 8 were unmarried; 24 asked for their mothers, and 4 for some other person; 10 did not specify whom they wanted. It is apparent from these results that few women wish to spend their labour in the company of their immediate family.

## BEHAVIOUR DURING LABOUR

### (a) *Time of Maximum Distress*

Before assessing reactions to labour, certain fundamental points were studied. A broad division of deliveries into night and day showed no increase of pain or fear among those occurring during the hours of darkness.

The most distressing period of labour was determined by asking each patient to mark one of five times between her admission and transfer to the lying-in ward. (Table III.)

A broad interpretation of these figures suggests that the end of the first stage is the most unpleasant period of labour for most cases. The first impressions of the labour ward upset more primiparae than multiparae. This was reversed for the delivery, 60 per cent of the patients in this group being multiparous.

### (b) *Companionship*

Being left alone during labour is generally thought to be one of the most unfortunate penalties of delivery in a busy hospital unit, yet in answer to a question on this subject, 340 (45 per cent) of patients expressed a desire to be left alone during the first stage. The number of primiparae (184) in this group, rather surprisingly, exceeded the multiparae (165). This high proportion is difficult to understand; probably some patients chose to be alone as an alternative to being with other patients in labour, rather than with a midwife or husband.

### (c) *Pain and Fear*

The evaluation of subjective symptoms is always difficult in clinical work. For this study, pain was assessed as a relative value, by asking each patient whether labour, as a whole, was more or less than expected; a third column was included for those who found it as painful as expected. This method is too general in its application, but it does indicate the collective success of preparation and treatment.

During this enquiry, sedatives and analgesics were given when required by the patient; nitrous oxide and trilene were also available on request. (Table IV.)

TABLE IV
*Pain*

| | Primiparae | Multiparae | Total |
|---|---|---|---|
| More painful than expected .. .. .. | 101 | 69 | 170 (22%) |
| As painful as expected .. .. .. .. | 157 | 165 | 322 (42%) |
| Less painful than expected .. .. .. .. | 142 | 133 | 275 (35%) |
| Not answered .. .. .. .. .. | 8 | 1 | 9 (1%) |
| Total .. .. .. .. .. .. | 408 (53%) | 368 (47%) | 776 (100%) |

These figures were taken from the impressions of the mother immediately after delivery. As it was thought that the appreciation of pain may alter later in the puerperium, 390 patients were asked the same question six days later. At this time 17 per cent had changed their minds. In about equal numbers the assessment of pain had increased or decreased.

In any study of pain, it is essential to consider its relation to fear. If this was absent, the patient was assessed as calm, if present she was graded into anxious, afraid, or hysterical. One record was made on admission and several during the later stages of labour. Where more than one observation was made, the highest degree was taken for classification. No case was included where observations were absent or incomplete. (Table V.)

More than 50 per cent of patients showed some degree of fear on admission, and this figure did not vary with parity. Multiparous patients, calm on admission, had a 67 per cent chance of remaining so throughout labour; however, this figure was reduced to 53 per cent for primiparae. There was a different pattern for patients showing fear on admission, improvement later in labour being greater among the primiparae (48 per cent) than the multiparae (23 per cent). Turning now to the question of patients who became more afraid as labour advanced, the position again varied considerably with parity. Among those patients who were calm on admission, 47 per cent of primiparae and 33 per cent of multiparae became afraid as labour progressed. The opposite was true for those patients who were anxious or afraid on admission, the increase in fear being greater among multiparae (35 per cent) than primiparae (25 per cent). These figures are difficult to explain but it is possible that a high proportion of the multiparous patients, who were already afraid on admission, were those whose previous obstetric abnormality had necessitated booking for hospital confinement.

TABLE V
*Fear*

| | | On Admission | Later in Labour | | |
|---|---|---|---|---|---|
| | | | Unchanged | Improved | Deteriorated |
| Calm | Primiparae .. .. | 146 | 78 (53%) | — | 68 (47%) |
| | Multiparae .. | 145 | 97 (67%) | — | 48 (33%) |
| Anxious or Afraid | Primiparae .. .. | 202 | 57 (27%) | 95 (48%) | 50 (25%) |
| | Multiparae .. | 168 | 71 (42%) | 38 (23%) | 59 (35%) |

TABLE VI
*Fear and Pain*

| On Admission | | Pain During Labour: More than Expected | As Expected | Less than Expected | Totals |
|---|---|---|---|---|---|
| Calm | Primiparae .. .. | 33 (23%) | 58 (41%) | 50 (36%) | 141 |
| | Multiparae .. .. | 24 (16%) | 68 (46%) | 58 (38%) | 150 |
| Anxious or Afraid | Primiparae .. .. | 52 (27%) | 77 (41%) | 61 (32%) | 190 |
| | Multiparae .. .. | 38 (23%) | 76 (45%) | 54 (32%) | 168 |

TABLE VII
*Relation of Pain to the Length of Labour*

| Duration of Labour (Hours) | More Painful than Expected | As Painful as Expected | Less Painful than Expected | Totals |
|---|---|---|---|---|
| 6 or less .. .. .. | 30 (14%) | 90 (41%) | 100 (45%) | 220 |
| 7 to 23 .. .. .. .. | 99 (23%) | 189 (45%) | 139 (32%) | 427 |
| 24 or more .. .. .. | 38 (35%) | 39 (35%) | 33 (30%) | 110 |

TABLE VIII
*Relation of Fear to the Length of Labour*

| Duration of Labour (Hours) | Calm | Anxious or Afraid | Totals |
|---|---|---|---|
| 6 or less .. .. .. .. .. .. | 115 (64%) | 64 (36%) | 179 |
| 7 to 23 .. .. .. .. .. .. .. | 170 (47%) | 192 (53%) | 362 |
| 24 or more .. .. .. .. .. .. | 31 (33%) | 64 (67%) | 95 |

TABLE IX
*Relation of the Length of Labour to Fear on Admission*

| Condition on Admission | | Duration of Labour: 6 Hours or Less | 7 to 23 Hours | 24 Hours or More |
|---|---|---|---|---|
| Calm | Primiparae .. .. .. | 23 (40%) | 85 (43%) | 34 (48%) |
| | Multiparae .. .. .. | 62 (51%) | 76 (45%) | 14 (51%) |
| Anxious or Afraid | Primiparae .. .. .. | 35 (60%) | 117 (57%) | 37 (52%) |
| | Multiparae .. .. .. | 60 (49%) | 91 (55%) | 13 (49%) |
| Totals | Primiparae .. .. .. | 58 (100%) | 202 (100%) | 71 (100%) |
| | Multiparae .. .. .. | 122 (100%) | 167 (100%) | 27 (100%) |

An attempt was made to compare the midwives' assessment of fear on admission with the patients' appreciation of pain after delivery. Six hundred and forty-nine cases were used. (Table VI.)

It can be seen that there is little variation with parity, and the pattern of pain and fear followed the expected course, namely, an increase in pain among patients showing some degree of fear.

In addition to these observations, each patient was asked to mention the most disturbing single subjective factor during labour. Four hundred and thirty-two (56 per cent) mentioned pain, 294 (38 per cent) fear or anxiety and 50 (6 per cent) some other factor. Thus, pain, fear and anxiety accounted for 94 per cent of the answers. It is interesting to note here that 133 (48 per cent) of the 275 mothers who found labour less painful than expected, indicated that pain, even so, was the most disturbing single factor. Amidst these very positive subjective symptoms, it was perhaps surprising to find 18 (2 per cent) mothers to whom boredom was the most disturbing factor.

(d) *Pain and Fear in Relation to the Length of Labour*

It has been suggested that pain increases with the duration of labour; however, the strength of individual contractions is often greater in short labours, while the intervals of relaxation are reduced, which suggests that pain in many of these cases should be more severe than in prolonged labours. On the other hand, though many long labours are associated with infrequent contractions of low magnitude, in others, a hypertonic state of the uterus may increase the degree of pain. If the individual contractions were equally painful in each group, the only variable factor would be time, and, indeed, it can be shown that an increase in the time of labour is accompanied by a corresponding increase in pain. (Table VII.)

No significant difference was found with parity, consequently all cases were considered together. As the time in labour increased, there was a rise in numbers in the more painful group and a fall in the less painful group. Thus, pain was found to be directly proportional to the time in labour.

If current impressions are correct, a similar pattern should be found when considering fear. (Table VIII.)

The figures showed that fear, as expected, ran parallel to pain, increasing in proportion to the length of labour. These recordings of fear were made late in labour, and it is therefore not possible to decide whether the length of labour was responsible for the fear or *vice versa*. Read (1933) supported the old adage, "A tense mind means a tense cervix", therefore, if one accepts that the tense cervix is associated with prolonged labour, a study of patients afraid on admission should show a high proportion in the longer labour groups. (Table IX.)

Many of the groups in this table are too small to be statistically compared, but the pattern as a whole, for both parity groups, suggested that the condition on admission bore no relation to the ultimate length of labour; indeed, in the primiparous group, the percentage of patients showing fear on admission progressively decreased with the length of labour.

(e) *Pain and Fear in Relation to Antenatal Exercises*

The reciprocal nature of pain and fear has never been disputed, yet, until the intensity of these symptoms can be accurately measured, no scientific comparison can be made. In this study, pain and fear ran parallel when all cases were considered together; however, in a selected group of primiparous patients, they were found to deviate. This group was composed of 143 patients who had attended relaxation classes and 265 patients who did not. In the relaxation group, 22 per cent of patients found labour more painful than expected against 26 per cent in the control group. At the other end of the scale, 30 per cent of relaxation cases found labour less painful than expected, against 42 per cent of control cases. Those who found labour as painful as expected were not considered. Thus, it can be seen that pain was not reduced by attending relaxation classes. These figures may indicate, however, that the present system of instruction leads the patient to think that labour is painless, and therefore, when she experiences pain, however slight, it is more than she had expected. On the other hand, the

uninstructed patient, fearing the worst, more frequently finds it is better than expected. The intensity of pain may well be the same in both groups.

Fear, however, showed a variation in these groups. Fifty-four per cent of the relaxation cases were calm on admission and indeed, remained so throughout labour; but this applied to only 37 per cent of the uninstructed cases. Among those patients showing fear on admission, 46 per cent of relaxation cases and 63 per cent of control cases, there was a 4 per cent improvement in the former group later in labour, but the latter remained unchanged. Therefore, in this instance, pain was unchanged whilst fear was reduced. This unexpected deviation of pain and fear is contrary to the teaching of Read (1933) who attached great importance to the "fear-tension-pain" syndrome. Of relaxation he wrote, "—if seriously and patiently applied, it can become one of the most pain-destroying agents during parturition".

Painless labour is achieved by only a small proportion of women. Teaching should always be applicable to the majority, and, possibly, it is wrong to emphasize the absence of pain in preparing the expectant mother for labour. A woman familiar with the nature of labour pains will be less afraid and better equipped to relax and co-operate during childbirth. Many patients must face disillusionment and a sense of failure when they realize in early labour that childbirth is not painless for them.

### Treatment of Symptoms in the First Stage

Many midwives are not fully acquainted with the actions of the drugs they use, and few have questioned the reasons for their administration. This frequently results in the use of sedatives, with little or no analgesic properties, in cases where pain is the predominant symptom.

During this series the midwives were asked to indicate a reason each time they used a drug, even if it bore no relation to the known action of the drug. An analysis of these reasons is shown in Table X.

With a more general classification, it can be shown that 96 per cent of the reasons fall into three groups:

(1) Pain Group (abdominal pain and backache) .. .. .. 574 (49%)
(2) Fear Group (fear, anxiety and hysteria) .. .. .. 299 (26%)
(3) Restlessness Group (restlessness and insomnia) .. .. 248 (21%)

Table X

*Reasons for the Use of Drugs on 1,175 Occasions in 776 Cases*

| | Primiparae | | Multiparae | | Total | |
|---|---|---|---|---|---|---|
| Abdominal pain .. .. .. .. | 271 | | 210 | | 481 | (41%) |
| Backache .. .. .. .. .. | 55 | | 38 | | 93 | (8%) |
| Anxiety .. .. .. .. .. | 127 | | 78 | | 205 | (18%) |
| Fear .. .. .. .. .. .. | 52 | | 21 | | 73 | (6%) |
| Hysteria .. .. .. .. .. | 10 | | 11 | | 21 | (2%) |
| Restlessness .. .. .. .. .. | 86 | | 48 | | 134 | (11%) |
| Insomnia .. .. .. .. .. | 64 | | 50 | | 114 | (10%) |
| Nausea or vomiting .. .. .. .. | 19 | | 10 | | 29 | (2%) |
| Other reasons .. .. .. .. | 15 | | 10 | | 25 | (2%) |
| Total .. .. .. .. .. | 699 | (59%) | 476 | (41%) | 1,175 | (100%) |

These figures suggest the need for three types of drug in the first stage; an analgesic for the pain group; a tranquillizer for the fear group; and a hypnotic for the restlessness group. Though most drugs in common use have a predominant action on one group, to a lesser extent, they encroach on the others. This is not always desirable, and in fact, 25 per cent of patients in this series complained that they were too sleepy during labour; only eight (1 per cent) felt that they were not sleepy enough.

## Analysis of Patients' Comments and Criticisms

One great disadvantage of any questionnaire is the fact that set questions are asked, leaving no channel for free expression. As already described, each patient was given the opportunity of writing, in her own words, her comments and criticisms. Three hundred and nineteen answers were received, varying in length from one word to several closely written paragraphs.

*General Classification*

| | |
|---|---|
| Subjective phenomena .. .. .. .. | 218 |
| Self criticism .. .. .. .. | 44 |
| Criticism of the staff or conduct of labour | 32 |
| Dislike of medical interference .. .. | 25 |
| Total .. .. .. .. .. | 319 |

*Subjective Phenomena*

Once again, pain and fear dominated these answers. Just the single word pain was used in 68 cases but, backache, bearing down, and crowning of the head were mentioned in another 35. Fear was unspecified in 55 cases. In the remainder it was related to the spontaneous rupture of membranes, the attempt to stop bearing down, the sight of the mask, and the lack of relief from gas and air. An interesting group of 8 patients found that fear for the life or normality of their baby caused the greatest anxiety throughout labour.

Twenty-five mothers were upset by the duration of labour; 22 by "the waiting" or "the length of labour"; and 3 by the rapidity of labour. There was no evidence of prolonged labours in the former, but the longest labour of the 3 in the latter group lasted eight hours.

*Self Criticism*

This interesting group revealed a form of stress during childbirth which is not often described. In these patients, the most disturbing factor was the feeling that they had failed in some respect during their labour. Failure to relax, lack of control, inadequacy and cowardice accounted for half the cases. The remainder were afraid of becoming a nuisance or upsetting other patients in labour.

*Criticism of the Staff or Conduct of Labour*

Noise, light, heat, overcrowding in the first-stage room, and too many people in the labour ward accounted for a third of these complaints. Another third concerned conflicting and inadequate instructions, or too many people issuing them. The remainder dealt with a variety of matters, ranging from late transfer to the labour ward to restriction of pain-relieving drugs. Even the standard sized labour ward bed came in for some criticism by 3 patients, who found it too small for safety. Only 4 (0·5 per cent) cases objected to the behaviour of the midwives. Though this figure is small, it could represent approximately 3,000 complaints throughout the country in one year.

*Medical Interference*

It is not surprising that the majority of patients in this group objected to pelvic examination. Treatment in the form of enemas, perineal repairs, blood transfusions, and surgical rupture of the membranes accounted for the other grievances.

## Conclusions

Pain and fear are the most distressing factors in labour, whatever the parity of the patient, being increased in direct proportion to the length of labour. Preparation for labour should be directed towards the relief of fear, and pain should be accepted as a frequent accompaniment of childbirth; its cause and control should be explained in books and lectures. By these means, fear will be reduced and the mother can

co-operate during labour, and, in doing so, her perception of pain should be lessened. By accepting pain, many mothers will be relieved of a sense of failure during their labour.

Neither the progress of labour nor the degree of pain can be altered by lectures or relaxation classes, but the reduction in fear must increase the confidence and co-operation of the patient, and this fact alone should be sufficient reason to encourage better attendances.

As far as the home environment is concerned, an effort should be made to restrain or rebuke the parous women who relate their unpleasant experiences to the unsuspecting primigravida.

The origin of many complaints can be traced to over-crowding, inadequate accommodation, or shortage of staff. In a Utopian state where these factors need not be considered, certain recommendations could be made. The labour ward should look more like a bedroom than an operating theatre, with sound-proof walls, indirect lighting, and controlled room temperature. The atmosphere should be one of quiet confidence and the number of people in attendance should be limited. Only one person should give advice, which should be clear and concise. Help in the form of reassurance or drugs should be available whenever requested. From the end of the first stage until delivery, the patient should not be left alone, as this covers the most distressing period, during which she needs constant support and encouragement.

The only justification for a husband's presence during labour is to support and comfort his wife, and this can best be done during the first stage. If an ideal relationship exists between husband and wife, he must be moved by her condition in the second stage; in such a state, he can only be an added burden to his wife and an embarrassment to her attendant.

Analgesic, hypnotic and tranquillizing drugs should be administered for the relief of the patient's symptoms and not only according to the dilatation of the cervix. The midwife should clearly understand the actions of the drugs she uses, and should record the reason for each administration.

In conclusion, it is true to say that there is no panacea for the woman in labour. Most of the Government recommendations are admirable, but it is not possible to fulfil them at the present time. The focus should be on the problems of staffing and accommodation: when these are adequate, the other improvements will rapidly follow, if a responsible professional enquiry is allowed to take the place of a public outcry based largely on ignorance and emotion.

## Acknowledgments

I would like to record my thanks to Mr. D. M. Stern and Mr. C. W. F. Burnett for their encouragement and advice on every aspect of this subject; to Dr. B. W. Cromie, Dr. H. Matthews and Mrs. P. MacFarlane for their help in preparing the subject matter; to the medical and maternity staffs of the West Middlesex and Chiswick Hospitals for their wholehearted co-operation, to the authors, editors and publishers of the various works quoted in this paper, and finally to Miss M. Green, S.R.N., S.C.M., without whose help this work could not have been undertaken.

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# REPORTS OF SOCIETIES

## NORTH OF ENGLAND OBSTETRICAL AND GYNAECOLOGICAL SOCIETY

JANUARY 1961

The Annual General Meeting of the North of England Obstetrical and Gynaecological Society was held in Manchester on 20th January, 1961.

The following were elected officers for 1961:

*President*—Mr. L. B. Patrick.

*Vice-Presidents*—Dr. K. V. Bailey (Manchester), Dr. W. J. Clancey (Sheffield), Miss G. Kay (Leeds), Mr. D. F. Smith (Newcastle), Mr. C. H. Walsh (Liverpool).

*Honorary Treasurer*—Mr. T. B. FitzGerald.

*Honorary General Secretary*—Mr. T. Smith.

*Honorary Reporting Secretary*—Miss U. M. Lister.

Mr. L. B. Patrick took over the Chair from the retiring President, Professor T. N. A. Jeffcoate.

Mr. R. M. Corbet read a paper

### CERVICAL CARCINOMA IN AN IDENTICAL TWIN

(This article appears on page 816 of this issue)

*Discussion*

The President asked if there were similar exogenic factors operating in the two cases.

Mr. G. A. Craig enquired if it was essential to perform a hysterectomy for carcinoma *in situ*.

In reply Mr. Corbet stated that both girls had lived similar lives and started childbearing at an early age. He did not consider hysterectomy usually necessary for carcinoma *in situ*. When the finding has been reported following amputation of the cervix he did not take further steps apart from follow-up. However, in the present case hysterectomy seemed desirable because of the extent of the carcinoma in the sister and because of the previous menorrhagia.

Dr. F. A. L. Da Cunha reported

### A CASE OF OVARIAN PREGNANCY

The patient, aged 19 years, had her last menstrual period 7 weeks before and 3 weeks after this had heavy bleeding for several days. Four days before admission to hospital, she fainted, and 2 days later developed lower abdominal pain associated with a brown vaginal discharge. The haemoglobin on admission was 53 per cent. A tender swelling could be felt in the Pouch of Douglas which on aspiration showed free blood in the peritoneal cavity. Laparotomy revealed a blood clot attached to the left ovary, from which blood was dripping into the peritoneal cavity. The left Fallopian tube was distinct and normal, and the right ovary contained a recent corpus luteum. Following removal of the left ovary the patient made an uninterrupted recovery.

In this case Spiegelberg's criteria were fulfilled and, in particular, the presence of ovarian tissue in the wall of the sac was demonstrated. The view is held by some that unless the gestation sac is found growing within a capsule of ovarian cortex and adjacent to a fresh corpus luteum, the case is not that of primary ovarian pregnancy, but extrusion of a tubal pregnancy which becomes adherent to the adjacent ovary. The alternative view holds that if the ovum be fertilized within the ovary, the ovum must have reached that stage of maturation normally found at the site of fertilization, and it is therefore unlikely that fertilization of the ovum occurs within its own follicle as maturation will not have occurred.

In the present case the histological slide shows that the corpus luteum adjacent to the gestation sac was not recent but organizing. The ovum probably originated in the fresh corpus luteum in the right ovary, migrated across the midline and became implanted on the left ovary, but it cannot be stated where fertilization occurred.

*Discussion*

The President had only recently seen his first case of ovarian pregnancy. The ovum seemed to be implanted on a thin layer of luteal tissue so that it was possible to excise the corpus luteum. Symptoms may arise early before even a period is missed.

Miss U. M. Lister showed slides of an ovarian pregnancy. The tube on that side was quite undamaged, but the ovary was 4 inches in diameter with numerous haemorrhages into its substance. At the centre of the ovary was the amniotic sac containing an 8-weeks foetus. This patient had noticed pain soon after a missed period, and though the enlarged ovary was felt it was impossible to arrive at the true diagnosis. Later a tender mass adjacent to the uterus led to immediate laparotomy when the ectopic pregnancy was seen to be ovarian and not tubal. There was no intraperitoneal bleeding.

Mr. T. F. Redman questioned if maturation of the ovum was in the tube or still *in situ*. He thought the polar bodies could be discharged and the ovum fertilized in the ovary.

Mr. T. B. FitzGerald thought the ovum could be fertilized in the ovary and the ovum could then escape, negotiate the tube, and arrive at the uterus, so accounting for failure of the "safe period".

Mr. C. de Boer described

### A GYNAECOLOGICAL CALCULATOR

This ingenious device consisted of a circular calendar over which there was a transparent cover fixed at the

centre so that it could rotate. A movable strip of celluloid also radiated from the centre and could be used to draw a line on the transparent cover. Setting this line against the date of the first day of the last menstrual period, further lines could be drawn to indicate the limits of the likely time of ovulation, or the time at which the patient should commence and end cyclical hormone therapy. With the next menstrual period the patient herself set the transparent cover so that the line representing the first day of the period came to the new date, thereby ensuring that the patient began and ended her treatment on the correct dates in relation to menstruation.

Mr. H. Arthur gave a short paper on

### Dehydration in the Aetiology of Pulmonary Embolism

The object of the paper was to stress the importance of dehydration leading to haemo-concentration in the aetiology of pulmonary embolism. By attention to the main aetiological factors, anaemia, trauma and sepsis, and by early ambulation, the risk of embolus has been markedly reduced. In both the patients to be reported attention was paid to pre-operative preparation, the first signs of sepsis were treated and they were both allowed out of bed soon after operation. Both these patients died from pulmonary embolus, and, from the histories, the common factor was dehydration.

The first patient, aged 53 years, was treated with two insertions of radium for Stage II carcinoma of the cervix. A month later she was admitted for Wertheim's hysterectomy. There was no anaemia at this time, but she was obese and had bronchitis. No particular difficulty was encountered during the operation though the glands on the right side were enlarged. After operation her chest gave some trouble, and though at first her urinary output exceeded her intake this was corrected by the third day. Her urinary output fell again on the 6th day, there was left-sided renal tenderness and intravenous fluids were given. Evidence of some dehydration persisted, and her abdominal wound required re-suture on the 11th day, but some 12 hours later she died from a massive pulmonary embolus. The original site of the thrombosis could not be found post mortem.

The second patient, aged 51 years, was treated by curettage and pelvic floor repair. Apart from mild hypertension her condition was good, and blood loss at operation was average. A urinary infection was treated at once. Post-operative vomiting persisted and on the 3rd day intravenous fluids were given for the next 48 hours. Her condition improved, she got up on the 6th day, though she had had bed exercises, but while sitting in a chair she collapsed from a pulmonary embolus.

Reviewing these cases it seems there was definite dehydration in the first patient, allowing haemo-concentration to occur early, and undue amounts of fluid were lost by respiration and through the skin. It is unlikely that secondary suture of the abdomen had any bearing on the outcome. Again in the second case persistent vomiting and insufficient fluid replacement led to dehydration and with it the risk of intravascular clotting and the formation of an embolus.

*Discussion*

The President agreed that there was evidence of dehydration though obesity and sepsis might be responsible.

Mr. F. Stabler was not convinced about the evidence of dehydration. He did not think this could be assumed from the intake, urinary output and appearance alone.

Mr. P. Malpas thought it illogical to believe that a diminished urinary output was a sign of dehydration. The interval of 2 months between the radium therapy and the hysterectomy was too long.

Professor T. N. A. Jeffcoate commented on the figure of one case of embolus in 2,500 operations. This applied to fatal cases and there were many more non-fatal cases. He had now had one fatal case in which he blamed obesity, reluctance to move, and shallow breathing. He thought the 6th day too late for getting up if embolus is to be avoided. Fatal embolus is as frequent in obstetric as in gynaecological cases and it is difficult to ascribe this to dehydration. There are certain countries where embolus is not seen, notably hot countries.

Dr. R. Newton thought the clinical estimation of dehydration impossible.

Professor W. I. C. Morris asked if Mr. Arthur was present at the post-mortem examination. He had seen a patient die after Caesarean section for placenta praevia, and the pathologist had removed numerous casts even from the smallest vessels indicating pulmonary thrombosis not embolus.

Professor C. S. Russell commented on the tendency in cases of carcinoma to venous thrombosis. In addition there had been the damage from radium and operation.

In reply, Mr. Arthur said these two patients had died in the same week and the aetiology of the embolus had been considered. The only common factor was the dehydration which he thought was evident not only from the falling urinary output but the appearance. In the second case there had also been vomiting, and though she did not get out of bed early she did have exercises. He would welcome a laboratory test which would indicate dehydration.

## NORTH OF ENGLAND OBSTETRICAL AND GYNAECOLOGICAL SOCIETY

### February 1961

A meeting of the North of England Obstetrical and Gynaecological Society was held in Liverpool on the 17th February, 1961. The President, Mr. L. B. Patrick, was in the Chair.

Mr. J. S. Scott presented a case record

### Recurrent Coagulation Failure in Pregnancy

A patient, aged 33 years, had experienced 7 unsuccessful pregnancies before delivering live babies in her 8th and 9th pregnancies. In her 10th pregnancy she was

seen when 19-weeks pregnant and had an apparently normal pregnancy, but later the same day the patient developed lower abdominal pain and fainted. This was followed by haematemesis, vaginal bleeding and the appearance of petechiae all over the body. Blood coagulation failure due to fibrinogen depletion was proved by laboratory tests. After transfusion of 2 pints of blood, the loss subsided. The fibrinogen level was restored to normal within 48 hours, foetal movements were felt and the pregnancy appeared to be continuing normally.

One month later the patient again developed lower abdominal pain, faintness and vaginal bleeding and again blood coagulation failure due to fibrinogen depletion was diagnosed. The coagulation failure corrected itself spontaneously and once more the pregnancy appeared to be continuing normally.

As further recurrence of the coagulation failure was feared, it was decided to terminate the pregnancy and this was achieved by oxytocin infusion. A live male child (weight 1 pound 1 ounce) was delivered and survived for 24 hours. The placenta, which followed rapidly, was ragged and showed some pale, and evidently old, blood clot adherent to one portion of the circumference with some fibrin deposition in this region. There was no evidence of recent abruption.

Immediately after the expulsion of the placenta there was loss of approximately 1 pint of clotted blood from the vagina and it was obvious from examining the placenta that a large portion was missing. Exploration under general anaesthesia produced a piece of placenta 2 inches in diameter from the uterine cavity. No tears were evident and the uterus was of normal shape.

Approximately 5 ounces of clotted blood was lost during this operation—making a total of 25 ounces. While being transferred back to the ward, and despite continuous oxytocin and ergometrine intravenous infusion, a massive post-partum haemorrhage occurred and the patient became pulseless. Transfusion under pressure was commenced into two veins. Uterine bleeding continued; it was noted that the blood was clotting adequately and the loss appeared to be entirely due to uterine relaxation.

Despite all measures, bleeding continued at a rate equal to, or greater than, blood replacement and the woman's death seemed imminent. Eventually, after 3½ hours, the uterine retraction became more sustained. This may have been encouraged by a hot intra-uterine douche continued for 20 minutes. At this time, adequate blood coagulation was clearly demonstrated by the fact that the douche was interrupted through the douche nozzle becoming blocked by clots. During the fifth hour after delivery only one pint of blood was lost and after this the loss gradually ceased. The patient had received a total of 17 pints of blood and 1½ pints of plasma together with 5 mg. of ergometrine and 30 units of oxytocin. That she had not been over-transfused was shown by the fact that the haemoglobin level, which had been over 70 per cent prior to delivery, was 57 per cent on the following day. The patient was discharged well 14 days after delivery.

*Discussion*

The President commented on the unique character of the case, and thought that he might have been tempted to perform a hysterectomy.

Mr. R. Corbet had twice been called to the theatre to try to stop the haemorrhage after a colleague had done a classical Caesarean section for placenta praevia. Two years later the classical Caesarean section was repeated, but towards the end of the operation there was bleeding both from the abdominal wall and *per vaginam*. A subtotal hysterectomy was done and 11 pints of blood were given before the bleeding stopped. Mr. Corbet had later been called to deal with bleeding from the cervical stump. Before operation the patient had been perfectly healthy, the clotting time was normal and there was no antenatal bleeding.

Mr. P. Malpas thought coagulation failure was more common than we realized explaining cases of antepartum haemorrhage. He knew of no record of recurrence in the same pregnancy.

Mr. S. Bender asked about the place of a hot intra-uterine douche. He had had several cases in which the bleeding had only stopped after a hot douche. The heat increased uterine contractility and the speed of coagulation, and the douche removed the blood clot.

Dr. Moss had seen bleeding from an abdominal incision after heparin had inadvertently been given in a blood transfusion.

Mr. S. Bender read a short paper on

## The Management of Primary Introital Dyspareunia

In primary introital dyspareunia the prognosis was often regarded as poor. It has been found, however, that in a large proportion of cases success could be obtained by a sympathetic approach, combined with dilatation of the introitus under anaesthesia, followed by the use of graduated dilators. Such treatment might be considered no more than reinforced simple, psychotherapy, but it was important to obtain and keep the patient's confidence. There were two causes of failure. In the wife it was usually because of a psychological factor too deeply ingrained to respond to such superficial psychotherapy. Even the psychiatrist found it difficult to make headway when a woman was wedded to her dyspareunia and determined to keep it. In a minority of failures the fault lay in the impotence of the husband. This too was almost always psychogenic, but the results of treatment were better here than when the wife had to be referred to the psychiatrist. In a series of 26 cases, 3 of the 5 failures were primarily on the part of the wife and for 2 failures the husband was responsible.

*Discussion*

The President thought that this was a subject that was not taught properly in the medical schools, and that premarital consultations should be encouraged.

Mr. F. Stabler found almost all cases were curable and everyone has his own approach. This always concerns

both the husband and the wife, and before anything is done he interviewed the husband. He insisted that coitus must take place immediately after the introitus had been stretched and he did not advocate dilators.

Sir Andrew Claye said that it was vital to realize this was a partnership, and that impotence might be secondary to repeated failure. He was not in favour of operations and dilators and thought suggestion could be effective.

Dr. W. Calvert was in favour of operation but not dilators. He found that the use of a condom often caused dyspareunia.

Mr. E. Parry-Jones read a paper on

### The Lymphatics of the Vulva

In an earlier paper it was shown that the superficial lymphatics reached the inguinal and femoral nodes by travelling up the length of the vulva, and not by going on to the thigh.

Patent Blue was injected intradermally into both sides of the vulva of a woman aged 83 who had carcinoma of the vulva. On the left side, where the inguinal glands were enlarged, the dye was restricted to the labium majus, but on the right the injection crossed the labio-crural fold so that the peri-labial skin received some of the injection. On the left the lymphatics were dilated and the spread was wide but nowhere was there any tendency to spread on to the thigh, but on the right a lymphatic trunk could be seen outside the vulva. It would appear, therefore, that even when the lymphatics are partly, if not wholly, blocked there is no tendency for the lymphatics to pass on to the thigh to reach their terminal nodes.

The blood supply of the vulva arises from the superficial and deep external pudendal vessels which supply the more superficial part of the vulva, and the internal pudendal vessels which supply the deeper layers of the vulva. It is, therefore, possible that some vulval lymphatics go deep into the pelvis to reach the internal iliac nodes rather than that all should go to the superficial inguinal and femoral nodes.

To investigate this problem Patent Blue was injected in patients about to have a laparotomy, and the lymph nodes along the course of the internal and external iliac blood vessels were examined for any evidence of the dye. No dye was found at intervals of 20 minutes to 4 hours after the vulval injection. The conclusion was reached that the dye was arrested at the first group of lymph nodes and the generalized skin colouring was the result of vascular absorption of dye at the injection site and at the first group of lymph nodes. Final proof of the arrest of the dye at the first group of lymph nodes was obtained at a radical vulvectomy operation where dye was found in the inguinal and femoral nodes but none in the external iliac groups.

The problem of the lymphatics of the deeper layers of the vulva still remained. Attempts were made to inject radio-opaque fluid directly into the lymphatics, but they proved impracticable. Because iron can be injected and stained for histological examination Imferon was first used. Amounts varying from ½ to 1 ml. were injected into the vulva intradermally, subcutaneously and by deep injection the day before laparotomy. One or two glands were removed from the external iliac area and the internal iliac vessels were stripped of fat and lymphoid tissue. In 19 out of 26 cases where Imferon was injected into the labium majus the subsequent histological examination of the lymph nodes revealed free iron retained by macrophages. No iron was found in the iliac nodes opposite to the side of injection, thus excluding the possibility of absorption from the vascular system. Iron was seen in both the external and internal iliac nodes after vulval injection, and, in one case where Imferon was injected into the upper part of the anterior aspect of the thigh, iron was present in the internal iliac nodes indicating a communication to this group. In an endeavour to confirm this point a triangular piece of tissue lying between the internal and external iliac vessel was removed. Dissection of this tissue seemed to indicate the lymph vessels converging on the common iliac and a small vessel crossing over to the internal iliac nodes.

It seems reasonably certain that the lymphatic drainage of the vulva goes both to the inguinal and femoral nodes and to the internal iliac nodes, thus demonstrating a superficial and a deep lymphatic network which communicates in the vulva.

*Discussion*

The President thanked Mr. Parry-Jones for this painstaking work of great practical importance.

Dr. R. Newton thought it usual to extend the dissection to the external iliac glands, but the patients were full of complaints after division of Poupart's ligament. He found it easier to approach the glands from within the abdomen.

Professor T. N. A. Jeffcoate doubted if a prolonged operation was a great advance. If a more local operation was not curative, he doubted if any benefit was to be gained by dissecting the external and internal iliac glands.

Mr. Parry-Jones, in reply, commented that though iron travelled to the internal iliac nodes, there was no reason to suppose the cancer cells would travel so fast. He thought it wrong to dissect the intra-pelvic lymph nodes.

Dr. R. E. Rewell contributed a paper on

### The So-called Mixed Tumours of the Endometrium

The so-called mixed mesodermal tumours of the uterus have been recognized as a valid group for many years. They are distinguished from endometrial adenocarcinomas on the one hand by their sarcomatous stroma and from endometrial sarcomas on the other hand by their containing glandular elements which form an undoubted part of the tumour, as well as by the variety of tissues which may differentiate within the stroma. That such a distinctive group exists is assumed as undoubted in such recent accounts as that of Taylor (1958), although rather earlier observers were at pains to demonstrate it as

recently as Tudhope and Chisholm (1934). Stromal metaplasia is to be expected in tumours of the endometrium, a tissue which, of course, arises from extracoelomic mesenchyme and the wonder is that it occurs so rarely. Considerable overlap between the groups of tumours would, however, be expected.

The commonest form of the tumours, as it is usually recognized, is clinically and on naked-eye examination very like sarcoma, while on section the stroma resembles fibrosarcoma and glandular elements are few, consisting usually of a covering of columnar epithelium on the surface and a few glands scattered beneath this. Rarely, however, even if the gross appearance is typical, the stroma may be much less like sarcoma in most of its extent and the glands far more numerous, indeed the first impression may be that the tumour is an adenocarcinoma, despite the gross appearance and even the fact that fragments may have been passed *per vaginam*. One personal case was diagnosed only in retrospect when review of the section of curettings revealed well-differentiated cartilage in the stroma of what had been thought by a junior to be a straightforward adenocarcinoma. Another was first suspected when fragments had been passed even though the sections of these could be diagnosed only as adenocarcinoma. At the other extreme what appears to be a typical fibro-sarcoma or myxo-sarcoma may, when a number of sections are cut, show a covering of columnar epithelium on the surface, perhaps in only part. Such a condition is comparable to the continuity of squamous epithelium on the surface of the rare "botryoid" sarcoma of the cervix in children. As mentioned already, the connective tissue element may be difficult to distinguish from the usual stroma of an adenocarcinoma, degeneration in which may be most confusing. Willis (1960) stresses this point, but he includes as adenocarcinoma one in which the stroma showed metaplasia to muscle. This occurrence would surely justify the diagnosis of mixed mesodermal tumour. Be this as it may the case shows how variable the borderline between the two tumours may be and how it can be drawn very differently by different observers. In cases of doubt the further course of the patient may resolve the problem, but the prognosis for mixed tumours is by no means as bad as is often made out. Thus in a recent example the tumour was found at operation to have invaded the wall of the bladder, but the patient is alive a year later. For the tumour with metaplasia to cartilage mentioned above, the patient is alive and well eight years after a panhysterectomy was performed.

These variations in the structure of the tumour have been encountered in a personal series of only seven cases. Sections of these were shown.

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*Discussion*

The President had seen 6 such cases in 10 years and 5 of these patients were dead. The remaining patient was treated by radiotherapy for a recurrence which was found 5 years after the original operation.

Mr. C. J. Dewhurst asked if metaplasia to striated muscle occurred.

Dr. Rewell had found striated muscle in only one specimen.

## NORTH OF ENGLAND OBSTETRICAL AND GYNAECOLOGICAL SOCIETY

### March 1961

A meeting of the North of England Obstetrical and Gynaecological Society was held in Sheffield on 17th March, 1961. The President, Mr. L. B. Patrick, was in the Chair.

Professor C. S. Russell recorded a case of

### Velamentous Insertion of the Cord

This case presented as one of placental insufficiency with velamentous insertion of the cord and probably complete obstruction to the placental circulation during the later contractions of labour when the foetal heart seemed to stop.

The patient was a primigravida, aged 36 years, who showed a slight rise of blood pressure, and at the 32nd week of pregnancy her child was noted to be small. A month later the pregnanediol excretion was below normal, 20 mg. per 24 hours, and it showed a further fall to 14 mg. per 24 hours. At the 37th week of pregnancy albuminuria was noticed, so that delivery was thought urgent.

The foetal head was deep in the pelvis with the cervix already 2–3 fingers dilated, but on sweeping the membranes there was a small amount of fresh bleeding which quickly stopped. Pains soon commenced. The foetal heart remained normal, though a little slowing during contractions was later recognized.

Six hours later the membranes were ruptured during an examination, and the foetal heart rate became alarming rising to 170 per minute between contractions, and then becoming seriously slowed. Fortunately the cervix was dilated so that the rapid delivery of the baby, weighing 3¼ pounds, could be effected. The placenta, weighing 11 ounces, showed a velamentous insertion of the cord 5 inches from the placental edge, and a small retroplacental clot. It was thought that as soon as the cushion of liquor was removed the foetal head pressed on the whole length of the vessels in the membranes so that during contractions the placental circulation ceased.

It was questioned if obstruction of the placental circulation caused immediate slowing of the foetal heart, what was the mechanism of this slowing, and what was its possible limit? Apart from severe anoxia

what other factors will slow the foetal heart, and is there any detectable difference between slowing following head compression and that of cord compression?

Illustrations of the foetal heart rate on a tape recorder were given.

*Discussion*

The President asked if the cord was round the body as in such cases distress is nearly universal, and a velamentous insertion of the cord increased the incidence of the cord being wrapped round the body.

Mr. L. Snaith asked if it was right to assume that a congenital heart lesion had no connexion with alterations in foetal heart rate. He cited such a case.

Mr. S. Way remembered a similar case in a patient with a cervical fibroid, in which the cord must have been compressed at the pelvic brim.

Mr. H. Agar thought sudden pressure on the cord would not alter the heart rate so dramatically, as at birth when the cord is tied there is no such change.

Dr. D. C. A. Bevis reported

### A Rapid Method for Cervical Cytological Staining

This simple staining technique was described by Nuri Sagiroglu in 1960, and the stain TMK 101 was made from Sheaffer's ink; Permanent Blue-Black 1·0 ml., Permanent Red (02) 0·1 ml. and water to 25 ml. The solution remained stable for 1 week.

The smear is made with an Ayre spatula and the slide placed immediately in a 4 per cent solution of TMK 101. Overstaining does not occur, and the slide can be examined in about 10 minutes using a drop of TMK 101 and a coverglass. If required for longer colourless nail varnish is used to seal the coverslip. As the dyes are alcohol-soluble it is possible to restain by the usual Papanicolaou technique. To keep the slides for about 10 months Apathy's medium can be used (Pantin, 1960). This technique is cheap, rapid and allows the clinician to examine the smear immediately.

#### References

Pantin, C. F. A. (1960): *Notes of Microscopical Technique for Zoologists*. Cambridge University Press, London. p. 20.

Sagiroglu, N. (1960): *Amer. J. Obstet. Gynec.*, **79**, 385.

*Discussion*

Dr. C. G. Paine thought the stain might be methylene blue and eosin. He wondered why speed to look at the smear was necessary.

Mr. S. Way saw the need for haste but the cell shape could be seen without staining. He fixed in Carnoy's solution and stained with Ehrlich's haematoxylin.

Dr. C. J. Dewhurst asked if other inks were effective.

In reply, Dr. Bevis said that when there was no help anything that saved time was useful. Other inks could not be used.

Mr. F. Stabler read a short paper

### Vaginal Adenomatosis

(This article appears on page 857 of this issue)

*Discussion*

The President thanked Mr. Stabler for these interesting cases and asked if there was any investigation into the vaginal pH.

Mr. D. Blakey had seen three similar cases. All were young parous women with profuse mucoid discharge and punctate vaginitis in the upper vagina. The small lumps were treated with diathermy.

Mr. J. M. Gate was most interested in the treatment. He thought silver nitrate might induce squamous metaplasia.

Dr. Senn had seen 3 similar cases. The first, a woman of 67 years, noticed bleeding and a mucoid discharge. A small mass was enucleated, the vagina was raw, but curettage revealed a carcinoma. The vaginal mass was reported as an adenomyomatous retention cyst. The second patient, aged 25 years, had used a close-fitting contraceptive cap. Three small masses were enucleated from the vagina, and there were also extensive granulations in the vagina. In the third case chronic cervicitis was found and retention cysts spread on to the vagina. These cysts were punctured with a diathermy needle.

Dr. W. Calvert asked if the cervical columnar epithelium spread on to the vagina. He had performed a hysterectomy on a patient who had sustained considerable cervical trauma.

Mr. F. Stabler, in reply, said that the pH had not been measured, but thought it would be alkaline. The skin was affected only by scratching. This condition was diffuse and not localized, and though adenomatosis might not be the best name it had been used by Bonney. Diathermy would only increase the rigidity and dyspareunia. In each case there was a clear area around the cervix indicating that there was no downward spread from the cervix.

Mr. D. H. Lees presented a paper

### Treatment of Carcinoma of the Vulva with an Assessment of the Results

(This article appears on page 730 of this issue)

*Discussion*

Mr. S. Way was not now in favour of being so radical. He thought the most important factor was the wide removal of the vulva because of pre-malignant lesions and new primary growths. Secondly there should be an extensive dissection of the superficial glands, and the least important was the dissection of the deep glands. With a very radical operation many died of the operation, though of those that recovered the survival rate was good. There was a great need to close the wound, especially as so many patients were elderly. He did not use skin grafts, and as many skin flaps depended on the deep epigastric artery, care must be taken not to cut it.

Mr. W. Hunter used skin grafts, and he also made use of the anterior abdominal wall.

## NORTH OF ENGLAND OBSTETRICAL AND GYNAECOLOGICAL SOCIETY

### April 1961

A meeting of the North of England Obstetrical and Gynaecological Society was held in Leeds on 21st April, 1961. The President, M. L. B. Patrick, was in the Chair.

Mr. J. Eyton Jones recorded

### A Case of Aorto-Duodenal Fistula

The patient, aged 62 years, had noticed slight bleeding 10 years after the menopause, and had no other symptom. Examination revealed a high blood pressure and a somewhat bulky uterus, and on curettage the appearance of the endometrium was typically malignant. Total hysterectomy with removal of the upper half of the vagina and bilateral salpingo-oöphorectomy was, therefore, carried out. There was little penetration of the myometrium by the growth.

Two years after the operation she complained of low backache, and, later that year, the pain radiated down the leg. Her appetite was poor and she had lost weight. Investigation failed to show any recurrence of the neoplasm. Nearly 3 years after the operation, her symptoms had become more severe, and the haemoglobin was only 52 per cent. A blood transfusion was given and, as treatment in hospital had improved the pain and her appetite, she was thought fit for early discharge. At 10 p.m. she was found to be collapsed with epigastric pain soon after defaecation. Epigastric tenderness and guarding were found, and the faeces gave a faint positive with haemotest. It was thought that a carcinoma of the stomach might account for her symptoms, even though a barium meal had earlier shown no abnormality.

Six hours later a fresh melaena stool was passed accompanied by a haematemesis of about one pint. Her condition improved after 3 pints of blood by transfusion, but she collapsed again with further melaena.

A laparotomy showed distension of the duodenum and small intestine with blood clot. On opening the duodenum, blood poured out and a fixed malignant mass at the duodeno-jejunal flexure was detected. An attempt was made to free the duodenum but the patient died on the table. Post mortem this mass was seen to be carcinomatous and ulcerating through to the third and fourth part of the duodenum, and also eroding through an atheromatous plaque to the aorta, so producing a fistula. Carcinomatous involvement of the para-aortic glands continued down to the bifurcation of the aorta.

Only two cases of aorto-duodenal fistulae were found in the literature. The first, reported by Hoyle (1949), was caused by a sewing needle, and was ultimately repaired. In the second, reported by Heinzmann (1959), an anastomotic ulcer developed 30 years after a partial gastrectomy. Though the long fistulous track could be ligated, the patient died of heart failure.

#### References

Heinzmann, F. (1959): *Chirurg. (Berlin)*, **30**, 235.
Hoyle, J. D. (1949): *Surgery*, **25**, 608.

#### *Discussion*

Mr. F. Stabler had seen a case of a fistula between the duodenum and superior mesenteric artery when on a ship bound for Gibraltar. He had a haematemesis of 28 pints, and, after transfusion, the fistula was closed. Unfortunately he died by the time they reached the Red Sea.

Mr. S. Madden described

### A Desmoid Tumour Complicating Pregnancy

The patient was first seen in 1954 when approximately 38 weeks pregnant in her first pregnancy. It was found difficult to feel the foetal head because of a tumour in the anterior abdominal wall, which extended up to the umbilicus. It was 3 inches in diameter, flattened with a fairly well defined edge, but it extended beyond the sheath of the rectus muscle. It was decided that the tumour should be dealt with after delivery, but a cord presentation was found making Caesarean section advisable.

The abdomen was opened through a left lower paramedian incision. The tumour, which was thought to be a desmoid, was proved to be arising in the rectus muscle, and it was found to be clear of the symphysis and not involving the peritoneum. A biopsy was taken, and then a living child delivered through a classical incision. The histological examination confirmed the diagnosis.

There was little change in the size of the tumour, and some 5 months after delivery it was decided to remove it. After excision of the desmoid tumour it was found possible to close the peritoneum. A defect in the anterior parietes measuring 5 by 3 inches was filled by a piece of nylon net sutured to the anterior rectus sheath and external oblique aponeurosis. The wound healed by first intention with good functional result.

The tumour weighed 235 g. and showed strands of fibrous tissue.

In 1957 the patient again became pregnant; she had a normal pregnancy and an easy labour at term.

#### *Discussion*

Mr. H. Doberman had seen a similar case in a woman 18-weeks pregnant. It had been noticed 18 months before and 18 months after delivery it had not been removed and had not grown in size.

Mr. H. Agar enquired how the nylon mesh was sterilized.

Mr. P. Barkla asked about subsequent stretching of the scar and Mr. G. W. Theobald asked if X-rays had any effect on this growth.

In reply, Mr. Madden said the nylon mesh was sterilized in a packet at 130° C., but he did not know the effects of X-rays on a desmoid tumour.

Mr. S. B. Herd reported on

## The Working of a General Practitioner Obstetrical Unit

The unit was built in 1938 for maternity work under the control of the local council and was maintained through the Medical Officer of Health. With the inception of the National Health Service, two consultant obstetricians and a paediatrician were appointed. Anaesthetists also became available. The unit serves a population of 100,000 with 46 doctors on the obstetric list.

The accommodation has been increased to 46 beds, and an antenatal clinic added. All patients are seen at the clinic by one of the consultant obstetricians, on booking and at the 36th week, and on the request of the patient's doctor. No difficulty has been experienced with regard to booking, the obstetrician's decision being accepted, though a limited number of patients are transferred on medical grounds to hospital. Routine tests are performed at the clinic, and many complicated cases such as toxaemias or breech presentations are accepted in the unit. This is possible because of the high standard of skill of the local doctors.

To admit abnormal cases to such a unit makes a greater demand on the consultant's time, and breech presentations and external version are a particular problem. Caesarean sections, forceps deliveries and other procedures are regularly carried out. There is a need for such services as anaesthesia and blood transfusion which are provided by a general hospital, and above all a skilled obstetric registrar.

*Discussion*

The President found the overall consultant cover greater than in other units, and commented on this subject coming to the front.

Sir Andrew Claye was appalled by the amount of work done which he thought was due to the consultant cover and quality of the general practitioners. He had had experience of such units, and found permanent nursing staff difficult to keep. A maternal death from ruptured uterus would not have occurred in a better equipped unit. Premature babies should be cared for in special units.

Mr. S. Madden found a similarity with his unit. The consultant must give much time and see many cases. A good relationship with the general practitioners is essential.

Mr. J. M. King thought such supervision would not usually be tolerated.

Mr. J. K. Wilson was the youngest member of this unit which delivers over 70 per cent of the women in the area. He felt strongly that the general practitioners should be part of a specialist unit.

Mr. G. W. Theobald said that the only criterion should be cold figures. The number of maternal deaths was much worse than in Bradford domiciliary cases. He thought all such units should be closed at once, and the Society should voice its disapproval.

Mr. H. V. Corbett commented on

## Reports on Confidential Enquiries into Maternal Deaths

The two confidential enquiries have been valuable, and Dr. Godber of the Ministry of Health has written that "the real advantage is that everyone concerned is now looking for his own mistakes. We are all bound to make mistakes, but their recognition must surely reduce still further the incidence in the future."

The reports are set out in sections giving the main causes of death under which the cases are examined such as toxaemia and haemorrhage. Avoidable factors in death from toxaemia centre largely on inadequate antenatal care. In some instances the degree of negligence seems unbelievable, but, in the second report, shortage of hospital beds was not mentioned though implied. Some mistakes were made from confusion of responsibility, and this may continue under present conditions. Avoidable factors were more frequent in the second report (55 per cent); there is slight deterioration in the care of pre-eclamptic toxaemia.

Avoidable deaths from haemorrhage, mostly post-partum haemorrhage with retained placenta, dropped in the second report, and the value of prophylactic ergometrine was clearly shown. It is remarkable how seldom the haemoglobin was recorded. The seriousness of accidental ante-partum haemorrhage may not at first be appreciated, so there was failure to call consultant help or the Flying Squad.

Deaths from pulmonary embolism scarcely permitted the suggestion of the avoidable factor. Cardiac deaths were of equal frequency in the two reports. There was a failure to appreciate the progressive nature of initial valvular disease, and the dangers of Caesarean section in these women were again stressed.

The death rates from Caesarean section in the two periods were 4 per thousand, and 3·5 per thousand. Performance of this operation by junior staff was to some extent responsible, and haemorrhage and shock remain the most important immediate causes of death, stressing the urgent need for the proper provision for blood transfusion and the correction of ante-partum blood loss.

There were only 5 deaths due to anaesthesia where the obstetrician had given the anaesthetic. In the second report the anaesthetic services were beyond criticism. In "sudden death", apart from conditions such as amniotic fluid embolism, which have recently gained recognition, the cause was seldom obscure. The report shows that rupture of the uterus is not yet an obsolete condition.

These reports fully justify the time and care taken over them. It seems inescapable that the incorrect booking for home or hospital confinement is partly due to an absolute shortage of beds in some areas, and that some areas need more beds than will allow for a 70 per cent hospital confinement rate.

*Discussion*

The President commented on the excellent review, but regretted time was too short for adequate discussion.

Dr. R. Newton praised the work of the junior staff.

## THE EAST ANGLIAN OBSTETRICAL AND GYNAECOLOGICAL SOCIETY

### April 1961

The Spring meeting of this Society was held at the Norfolk and Norwich Hospital on Saturday, 29th April, 1961, with the newly-elected president, Mr. F. R. Stansfield, in the Chair.

The retiring president, Mr. Michael Bulman, gave his address on

### Forty Years of Obstetrics

When I joined the staff of the Norfolk and Norwich Hospital in 1924 there was no maternity unit, and patients requiring a Caesarean section were dealt with in the general surgical wards. Eventually the management committee converted a room in an attic into a seven-bed unit, and then in 1930 a thirty-bed maternity unit was built. At that time there was no effective treatment for puerperal sepsis and such therapy as was possible consisted of supporting the patients' natural resistance to the disease and administering large libations of brandy. In 1931 Dr. Leonard Colebrook put forward his droplet theory of infection and advised the use of masks in order to reduce the incidence of infections with the prevalent haemolytic streptococcus; in 1936 the introduction of Prontosil Rubrum provided the first effective remedy against this micro-organism.

In the following years came the discovery of other and more effective sulphonamide derivations and in 1941 the first of the antibiotics, penicillin, was introduced into clinical medicine in a crude form that gave many unpleasant reactions. Now that the bogey of puerperal sepsis was passing, it became safe to extend the range of indications for forceps deliveries, for Caesarean sections, and for manual removal of the placenta, which hitherto had been severely restricted, and this extension proved a boon to both mothers and their babies. Since the introduction of the sulphonamides and later the antibiotics the haemolytic streptococcus has lost its pre-eminence as a cause of puerperal infections to the haemolytic *Staphylococcus aureus*, which is a much more difficult micro-organism to control.

I am of the opinion that prolonged retention of the placenta will lead to profound shock and therefore advocate its early removal. In my student days every obstetric textbook carried a list of relative and absolute indications for Caesarean section; in those days the classical operation was fraught with considerable hazard. The introduction and popularization of the lower uterine segment Caesarean section operations by Munro Kerr of Glasgow and by De Lee in America reduced the immediate risks from sepsis and the remote risk of rupture of the uterine scar in a subsequent pregnancy so that Caesarean sections could be resorted to more readily with an improvement in the results for the mother and her baby. Now that the operation is easy and safe there is probably a tendency to resort to this solution of an obstetric difficulty too readily, when a little more delay on the part of the obstetrician might allow of a vaginal delivery. There is a risk that uterine inertia and foetal distress may be diagnosed on inadequate evidence and an operative delivery of the mother carried out unnecessarily. On the credit side I may mention that rarely nowadays does one perform perforations of the foetal skull, embryotomies, or decapitations and then never on a living child.

Up to the time of the last war blood transfusion was a difficult and hazardous undertaking, and I relied on normal saline injections. If given rectally, they usually were messy and acted as enemata. The discovery of the Rhesus factor in red blood cells by Wiener in 1941 and the war-time introduction of the blood bank and its successor the National Blood Transfusion Service have revolutionized obstetrics and justify the freer use of blood transfusion.

We have not advanced in our basic knowledge of the causation of toxaemia of pregnancy, but we have slowly improved in our methods of treatment and advanced from purgation and colonic lavage *via* Stroganoff's method to treatment with bed rest, sedation, and diuretics. I never could understand or approve of the use of chloroform as advocated by Stroganoff. I believe that there are two types of toxaemia, one that rapidly worsens into eclampsia and does not recur in subsequent pregnancies and the other that is milder, does not lead to convulsions, and tends to recur in later gestations. I am not convinced of the value of recording the patient's weight gain during her antenatal care.

In 1917 the use of X-rays in midwifery was unknown and one attempted external pelvimetry in an attempt to assess the size of a woman's pelvis. Then came the introduction of the use of X-rays for the diagnosis of twin pregnancy, for accurate mensuration of the pelvis, and for placentography. Recently fears have been expressed about the use of X-rays during gestation, and I now tend to restrict their use to obtaining a lateral view of the woman's pelvis.

The premature induction of labour has been a feature of British Obstetrics for many years and I remember using the stomach tube method, sea tangle tents, and Krause's bougies. Latterly I have restricted myself to the use of the Drew Smythe catheter for rupturing the hindwaters, although in some cases the forewaters are accidentally ruptured. The difficulty with this simple procedure is the uncertainty of its success in inducing labour and the very variable delay between the rupture of the membranes and the onset of labour introduces the risk of infection.

In concluding I must pose the question as to whether, with our modern scientific approach to midwifery and our modern maternity units, we are not losing some of the

commen human homely touch of the older and less efficient Maternity Home of former times.

*Discussion*

Mr. Lloyd, Mr. O'Meara and Miss Bottomley all favoured induction of labour by rupture of the bag of forewaters, and Mr. Carlisle reported a death from fulminating septicaemia after the use of a Drew Smythe catheter. Mr. Spry-Leverton, who had been Mr. Drew Smythe's Registrar, still favoured the use of his catheter and Mr. Carron Brown reported a case of accidental haemorrhage following its use. Mr. Carron Brown favoured early removal of the placenta although he knew of a case from the Flying Doctor service in Australia where the placenta had been retained three months.

In reply Mr. Bulman advised leaving the totally adherent placenta, but in all other cases its early removal was advisable, and he saw no reason why general practitioners and midwives should not perform the operation in an emergency.

Miss Bottomley, Mr. Lloyd and Mr. Bentall all favoured the use of ergometrine with hyalase at the end of the second stage of labour, and Miss Bottomley, Mr. Harrison, and Mrs. Townsley stressed the need for the Flying Squad to go out to all cases of retained placenta.

Mr. Spry-Leverton reported that they had halved their incidence of post-partum haemorrhage at Peterborough by the use of Mr. Kimbell's technique.

The Chairman closed the meeting after thanking Mr. Bulman for his address and for his work for the Society over the past five years.

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## ROYAL COLLEGE OF OBSTETRICIANS AND GYNAECOLOGISTS

27 Sussex Place, Regent's Park, London, N.W.1

THE following Lectureships and Prize are available in 1962:

### WILLIAM BLAIR-BELL MEMORIAL LECTURESHIP IN OBSTETRICS AND GYNAECOLOGY

The conditions of these appointments according to the bequest are as follows:

(*i*) Two lectures only may be delivered in each year.

(*ii*) The Lecturer must be either a Member of the Royal College of Obstetricians and Gynaecologists or a Fellow of not more than two years' standing. If the Council of the College think fit, two Lecturers may be chosen.

(*iii*) The subject or subjects of the Lectures must be either Obstetrics or Gynaecology, or closely related thereto. In the selection of the Lecturer or Lecturers, preference will be given to the Lectures embodying original work, particularly in regard to the morphology, physiology and pathology of the female reproductive organs, but this condition need not be considered an absolute condition of the appointment, particularly if the alternative be a problem connected with malignant neoplastic disease.

The honorarium for each of the two Lectures is twenty-five guineas.

*Recommendations* or *applications* accompanied by a short précis of the proposed Lecture, may be submitted to the Secretary at any time. The précis should bear a nom-de-plume.

### EDGAR-GENTILLI PRIZE

Through the generosity of Mr. and Mrs. Gilbert Edgar, the Council is able to offer annually a prize of £100, this to be known as the Edgar-Gentilli Prize. The award will be made in recognition of original work on the cause, nature, recognition and treatment of any form of cancer of the female genital tract, including chorioncarcinoma. Every fifth year the subject will be restricted to chorion-carcinoma and this restriction will next apply in the year 1966. Candidates for the prize should submit results of their researches in the form of an essay or article, written in English, and not previously published. Candidature is not restricted to Fellows and Members of the Royal College of Obstetricians and Gynaecologists. Applications for the next award should be sent to the Honorary Secretary on or before 1st February, 1962.

# BOOK REVIEWS

"Foetal Electrocardiography." By S. D. LARKS, Assistant Professor of Biophysics, School of Medicine, The University of California. Pp. 109, with 70 figures. Blackwell Scientific Publications Ltd., Oxford, 1961. Price 52*s*.

THIS is a comprehensive monograph on the uses of foetal electrocardiography, with a short historical introduction and useful bibliography. The technique of foetal electrocardiography, developed by Professor Larks and the Los Angeles Group, is fully described and illustrated.

First there is the diagnosis of foetal life at the early stage of 11 weeks, and from this time tracings can be made at intervals during the whole pregnancy to observe the effects of changing environment, pregnancy complications and labour. In early pregnancy, when doubts as to viability exist, as in threatened or missed abortion, an E.C.G. can confirm foetal life, although a negative finding may have no meaning as tracings are not always possible; and in the difficult diagnosis of hydatidiform mole a positive foetal heart tracing excludes this complication. Serial electrocardiographic studies of the behaviour of the foetal heart in pregnancy complications such as diabetes and Rh incompatibility may, it is mentioned, reveal abnormalities which may appear with sudden disaster to the foetus. The method obviates the use of X-rays in the diagnosis of multiple pregnancies and breach presentation.

The book states that the percentage of positive recordings of the foetal heart by electrocardiography reaches 50 per cent by the 15th week, is 100 per cent accurate by the 22nd week and that the accuracy decreases to 50 per cent at about the 30th week or 31st week, but once again returns to about 97 per cent accuracy by the 35th week.

During labour the electrocardiogram is shown as an additional instrument for providing new information as to the behaviour of the foetal heart and its response to maternal analgesia and the stress of delivery.

Illustrations are given of alterations in foetal heart rate. For early diagnosis of foetal distress this method is shown to be of immense value.

The value of electrocardiography in diagnosing foetal heart abnormalities is also illustrated, but foetal P or T waves are difficult to demonstrate with any consistency and this places a limitation on the method. It is hoped, however, that future improvement in technique may remove this limitation.

The method described by the author shows the maternal QRS complexes. These maternal complexes can be cancelled out, however, by other instrumentation leaving only the foetal complex. By another method foetal heart tracings can be presented to a counter and registered by a rate meter.

There is little doubt, as Professor Larks stresses, that any new information which saves a foetal life and leads to a successful termination of pregnancy and delivery is a victory for modern medicine. This is especially true in the common complication of foetal distress where irregularities of heart rate with profound tachycardias and bradycardias are common. The book, therefore, is to be welcomed as a valuable contribution to the provision of a better understanding of the action of the foetal heart and for its description of a method of lowering foetal mortality and morbidity. Once again is emphasized the inadequacy and limitation of random sampling of the foetal heart rate by a stethoscope during labour.

*D. J. MacRae*

"The Placenta and Fetal Membranes." Edited by CLAUDE A. VILLEE. Pp. xx+404, with 87 figures. The Williams and Wilkins Company, Baltimore, 1960. Price £4.

DR. VILLEE is to be congratulated on the orderly assembly of the proceedings of a Conference held at Princeton, N.J., in November, 1958, sponsored by the Association for the Aid of Crippled Children, which embraces current research into placental function. The book is in four parts, the first two reporting the proceedings of the Conference, the third part being an annotated bibliography on modern placental research, and part four detailing research in progress throughout the world on placental function.

In part one, eight reviews are presented by Amoroso, Dempsey, Ramsey, Barron, Brambell and Hemmings, Dancis, Villee and Hertig, and they cover the recent literature on hormone function, histochemistry, placental circulation, gaseous exchange, antibody transmission, the mechanism of foetal nutrition, biochemistry and pathology of the placenta. At the end of each review there is an extensive bibliography.

Part two is a report of the Conference during which each review was thrown open for discussion. Those participating included Boyd, Dawes and McCance from the United Kingdom. There was general agreement throughout the Conference proceedings that we must give up all ideas of the placenta being an organ working by simple diffusion and realize that it incorporates probably all the complex functions of respiration, nutrition and excretion exhibited by the adult organism. The big problem at the moment is to separate out these functions and to find out where, exactly within this complex organ, structure is related to function. The discussion is full, free and very instructive to all interested in the enigmas that surround the study of the placenta, and it is apparent

that though the morphologists have their problems despite histochemical analyses and the electron-microscope, the physiologists are battling with serious technical difficulties when it comes to the study of the human placenta. At present we must be satisfied with much information that comes from other mammals. Page describes the artificial womb set up in San Francisco for the study of transport phenomena, but the opinion was expressed that these perfusion experiments were carried out under conditions which were far from physiological.

Part three is a survey of the literature on the placenta and foetal membranes from 1946–58 and provides the main references in the world literature to anatomy, physiology, biochemistry, endocrinology, nutrition, pathology and published books. That this section covers some 117 pages is sufficient to explain the scope of this portion of the book.

Part four is a study of current research on the placenta and has been published separately. This is available, without cost, to any interested person upon request to the Association for the Aid of Crippled Children, 345 East 46th Street, New York, 17, N.Y. Only the list of investigators and their projects is included in the pages of the book reviewed.

Dr. Villee and all who contributed to this book must be congratulated on the assembly of all the available important and relevant material about the placenta to almost the date of publication of the book. The contents of the book illustrate how very difficult it is to develop new techniques for the study of human placental function, and it is in fact amazing how much has been done, despite many problems.

The book is published on good paper with large print, and is easy to read and it is extremely fitting that it should be dedicated to the memory of Streeter and Wislocki who contributed so much to embryology and placentology and who stimulated so much interest in their junior colleagues, many of whom took part in the Conference.

"Modern Trends in Urology." Edited by SIR ERIC RICHES. Second Series. Pp. 287. Butterworths Scientific Publications. Price 70*s*.

IN this book a team of experts presents the advances in urology made since 1953. The gynaecological aspects have not been accorded the separate chapter they enjoyed in the First Series, but relevant progress in this field has not been neglected by the editor, Sir Eric Riches.

The isolated ileal loop, a surgical Pooh Bah, is described in the roles of conduit, ureter and bladder. Opened into a flat graft it also enlarges the contracted bladder. Metabolic disturbances which follow diversion of urine into the intestine are defined and correlated with emergency and maintenance therapy. That ambitious modern project, renal transplantation, is described together with its immunological problems and current limitations. The recent break through in human genetics is included, especially in relation to Klinefelter's and Turner's syndromes. The chapter on the treatment of acute renal failure is worthy of special praise, the roles of dietary control and haemodialysis being clearly indicated.

Although most of this book is concerned with the kidney and with male urology there is much of interest to the gynaecologist. For in addition to the matters mentioned above there are descriptions of ureterocele, sarcoidosis and incontinence due to neurological disorders. The section on stress incontinence includes a detailed description of retropubic cystopexy by the original Everard Williams technique. Hyperfunction states of the adrenal cortex and medulla are included together with the methods of investigation and treatment. The book is well produced and will appeal to the urologically-minded gynaecologist.

"Management of Obstetric Difficulties." Revised by J. ROBERT WILLSON, M.D., M.S. Sixth edition. Pp. 687. Illustrated. The C. V. Mosby Company and Henry Kimpton, London. 1961. Price 123*s*. 6*d*.

IT is six years since the last edition of this book appeared. Much of the material has been re-written and new illustrations added. It is a book designed for the specialist in training and the practising obstetrician rather than for the medical student. The sequence of chapters is excellent—starting with two chapters on infertility and proceeding through pregnancy complications to labour and the puerperium. There are few complications that are not discussed and key references are given at the end of each chapter. The style is very American but the British literature is not ignored and the British reader will be impressed with the straightforward presentation and the ease of reference. The illustrations, both photographs and drawings are excellent. The book can be recommended with confidence as stimulating and instructive collateral reading.

"Clinical Obstetrics and Gynecology." Vol. 3, No. 4. "Fetal Physiology and Distress." Edited by THADDEUS L. MONTGOMERY. "Endocrinology." Edited by ROBERT B. GREENBLATT. Paul B. Hoeber, Inc., Baltimore. 1960. Subscription only: $18 per annum.

THIS quarterly publication which has now completed its third year is, as yet, insufficiently well known. It is a cross between a journal and a textbook. Purchase is by annual subscription only and there is no advertising matter. Each number consists of reviews or symposia on two subjects. The March, 1960 number which was reviewed in this journal, contained symposia on Obstetric Emergencies and on Paediatric Gynaecology. In June, 1960, the subjects were The Physiology of Pregnancy and Endometriosis. In September, 1960, there was a symposium on Bleeding in Late Pregnancy and a series of special articles on Frigidity and on historical subjects. The December number here reviewed carries articles on Foetal Distress and Physiology and a symposium on Endocrinology.

For the whole year there are 1,144 pages, including valuable bibliography and a cumulative index. The editors of the symposia and the authors of the individual articles are all well-known authorities on the subjects chosen, and for the busy specialist these periodic reviews make an easy and most satisfactory way of keeping up to date with current views.

"A Text Book of Midwifery for Students and Practitioners." By R. W. JOHNSTONE. Eighteenth edition, revised in collaboration with R. J. KELLAR. Pp. 592, with 302 illustrations and diagrams. Adam & Charles Black, London. 1961. Price 45*s*.

THIS textbook was first published 48 years ago. The continuing demand for it has necessitated eighteen editions. This in itself is sufficient evidence of its merit. The latest edition has been subjected to extensive revision and should therefore be judged by modern standards.

A great deal of the older material has been retained but there have been several additions which, although brief, are extremely acceptable. The re-written chapter on the toxaemias is excellent, as is that on radiography. In spite of this the result is somewhat disappointing and this disappointment stems from the mode of presentation rather than the content. For example, there is an impression of adherence to destructive operations which is quite unjustified by the text.

Other points are perhaps more controversial. Is it really safe or necessary to advise forceps rotation "only after efforts at manual rotation have failed", particularly when a very sound paragraph on Kielland's forceps is to be found on the next page? Does reposition of the cord really warrant such an unqualified description, even though it follows an admission that in hospital early cases are always treated by Caesarean section? The explanation for these discrepancies probably lies in the aim of the authors. Conditions in outlying districts in Scotland may still require occasional heroics, but these circumstances are rare in most other districts, and this should be made clear.

The book will still gain general acceptance amongst students. It remains a convenient size and the illustrations are helpful and adequate, without being expensive or elaborate. If read with care it will prove most instructive.

*D. N. Menzies*

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## THE NUFFIELD FOUNDATION
## NUFFIELD INSTITUTE FOR MEDICAL RESEARCH

### RESEARCH FELLOWSHIP

THE Nuffield Foundation, as an experiment, is prepared to offer one research fellowship in 1962, tenable at the Nuffield Institute for Medical Research at Oxford, to enable a suitably qualified person who intends to follow an academic career in obstetrics or paediatrics in the United Kingdom to concentrate for a year on animal experiments directly related to basic physiology or pharmacology in the foetus or the newborn.

The fellowship will be tenable for one year and is limited to a graduate in medicine of a University within the British Commonwealth, who should either have completed an appointment as Registrar (or its equivalent) in an approved department of obstetrics or paediatrics, or be seconded for one year from such an appointment. He should also have obtained the higher qualification appropriate to his chosen speciality. The stipend will be within the approved range of salaries for Senior Registrars under the National Health Service. Applications for the award beginning in 1962 must be received before 15th February, 1962, by the Director, The Nuffield Foundation, Nuffield Lodge, Regent's Park, N.W.1, from whom full particulars and application forms can be obtained.

L. FARRER-BROWN,
*Director of the Nuffield Foundation*

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## THE NUFFIELD FOUNDATION

### MEDICAL FELLOWSHIPS

As part of its programme for the advancement of health, the Nuffield Foundation is prepared to award a number of fellowships to men and women of the United Kingdom highly qualified in medicine, usually between the ages of 25 and 35, who wish to train further for teaching and research appointments in any branch of medicine.

Applications for awards in 1962, which must first be endorsed by the executive authority of a university medical school in the United Kingdom, must be received by the Foundation not later than *1st February, 1962*.

The conditions of these fellowships and the application forms are obtainable from the Director, The Nuffield Foundation, Nuffield Lodge, Regent's Park, London, N.W.1.

L. FARRER-BROWN,
*Director of the Nuffield Foundation*

# REVIEW OF CURRENT LITERATURE

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## PHYSIOLOGY

229. **Secretory Behaviour of Endometrium in Tissue Culture.**

By R. L. EHRMANN, H. A. MCKELVEY and A. T. HERTIG. *Obstet. and Gynec.*, **17**, 416–433. Apr. 1961. 20 figs. 10 refs.

Endometrial transplants from 19 hysterectomy specimens and 1 curettage were grown in organ culture on nutrient agar containing human cord serum or Trowell synthetic medium T.8 and studied histologically after varying periods of cultivation.

New glycogen-containing secretory vacuoles appeared in most of the explants within the first 48 hours, followed by lumenal secretion, and disappearance of secretory activity usually by the fifth day of cultivation. This secretory episode was independent of the phase in the menstrual cycle at which the endometrial explants were taken and occurred in the total absence of oestrogen or progesterone, and the incorporation of these hormones in the medium did not alter the secretory episode.

The ability of endometrium to secrete in the absence of ovarian hormones suggests that these hormones act *in vivo* by an indirect route. *J. G. Dumoulin*

## PREGNANCY

230. **The Pre-Diabetic Syndrome in Pregnancy.** (Das Prädiabetische Syndrom in der Schwangerschaft.)

By H. DIETEL. *Zbl. Gynäk.*, **83**, 773–778. May 20, 1961. 1 table. 1 fig. 24 refs.

As the maternal and foetal hazards during the pre-diabetic state almost equal those of diabetic pregnancy, it would seem desirable to develop methods of diagnosing the pre-diabetic state early enough to forestall them. With this object in mind the author investigated by means of a glucose tolerance test "a large number" of normal pregnant women as well as women with a history suggestive of the pre-diabetic syndrome. This method failed to reveal any cases of pre-diabetes even when applied to 37 mothers whose child weighed more than 10 pounds.

The effect on the blood sugar after the administration of cortisone or prednisolone yielded equally inconclusive results in 25 healthy non-pregnant women, 36 healthy women in the third trimester of pregnancy, and 22 pregnant women suspected of being in the pre-diabetic state. It would appear that there is as yet no satisfactory method of diagnosing this condition at a stage sufficiently early for effective treatment. *Bruce Eton*

231. **Assessment of Renal Function in Pregnancy.** (Zur Nierendiagnostik in der Schwangerschaft.)

By F. GÖTZ and T. PÖSCHEL. *Zbl. Gynäk.*, **83**, 664–672. Apr. 29, 1961. 2 tables. 3 figs. 34 refs.

Failure to recognize and treat sub-clinical infections of the urinary tract may eventually result in pyelonephritic small contracted kidneys. The authors studied a series of 100 pregnant women with indigo-carmine and phenol red excretion tests and Volhard's concentration test. Renal function assessed by Volhard's test was regarded as normal if a specific gravity of 1,025 was

reached. With indigo-carmine excretion begins in healthy non-pregnant women within 3–5 minutes, but in pregnancy a delay of up to 10 minutes should be considered as normal.

A comparison was made between one group of normal cases and a second group of women whose urinary sediment revealed the presence of infection, or who gave a history of previous disease of the urinary tract. In the second group a delay in indigo-carmine excretion was found in 50 per cent on the left side and in 30 per cent on the right side. Seventy per cent of patients with a past history of renal disease, including pyelitis, showed evidence of impairment of renal function as assessed by the concentration test. The phenol red test which in healthy non-pregnant subjects yields after 15 minutes an excretion of at least 35 per cent was found to drop to 24 per cent in 64 healthy pregnant women and to 17 per cent in 22 cases of pyelitis. There was, however, a considerable scatter of results which indicated that this test is not very suitable in pregnancy. *Bruce Eton*

232. **Use of Diethylpropion Combined with a Supplement for Safe and Effective Weight Control in Pregnancy.**

By M. J. JORDAN and G. M. BADER. *Surg. Gynec. Obstet.*, **112,** 663–666. June 1961. 1 table. 7 refs.

The authors discuss the use of a new appetite-depressant drug, diethylpropion, in weight control in pregnancy. Advantages claimed over d-amphetamine sulphate are the absence of cardiac toxicity, minimal effect on the blood pressure, minimal central nervous system stimulation and a more prolonged effect.

Studying the effect on 50 gravid women who were unaware that they were taking an appetite-depressant drug and who were on no dietary restriction, the authors found that, with a dose of 25 milligrammes three times daily, one hour before meals, a fourth dose being given in mid-evening if required, the average weight loss was 0·24 pound weekly. No side-effects were encountered.

*A. E. R. Buckle*

233. **Etiology of Hypertension in Toxemia of Pregnancy.**

By C. A. HUNTER and W. F. HOWARD. *Amer. J. Obstet. Gynec.*, **81,** 441–450. Mar. 1961. 12 figs. 15 refs.

Muscle strips from rabbit's aorta were used for assay of the effects of plasma and decidual extracts, as well as extracts of hydatidiform mole, on contractility of smooth muscle. A pithed nephrectomized cat was used for studying their vasopressor effects, a continuous blood pressure recording being obtained by a mercury manometer connected to a cannula in the carotid artery.

Addition of decidual extracts from patients with molar pregnancies and pre-eclamptic toxaemia caused contraction of the muscle strip and demonstrated the presence of a constrictor substance. No such contraction was got on addition of a decidual extract from a non-toxaemic mole. A vasoconstrictor effect was also demonstrated in pre-eclamptic plasma. This was not destroyed by boiling the plasma.

That the constrictor substance is also vasopressor was shown in the cat preparation where rises of 15 to 50 mm. Hg followed injection of decidual extract from molar pregnancy with pre-eclamptic toxaemia or of pre-eclamptic plasma. A fall of blood pressure, amniotic fluid pressure and uterine tonus followed withdrawal of liquid amnii in toxaemic patients.

The pressor substance is similar to hysterotonin and the authors believe that hypoxia is the cause of its formation in the decidua in toxaemia of pregnancy. With the release of pressor substance into the maternal circulation vasoconstriction is produced.

*F. J. Browne*

234. **Renal Glomerulo-Tubular Mechanisms During Toxaemia of Pregnancy.**

By M. J. LAMKEE and G. E. BRATVOLD. *West. J. Surg. Obstet. Gynec.*, **69,** 121–128. Mar.–Apr. 1961. 19 refs.

Seventy-five patients with toxaemia were studied in the University of Washington. The glomerular filtration rate and the renal plasma flow were measured and found to be 25–30 per cent below that of normal pregnancy at the corresponding period. The glomerular filtration rate is usually more depressed than the renal plasma flow. After delivery both these indices rise rapidly and attain the normal values within 5–12 days (the normal pregnant patient regains normality within 3 days). The filtration factor (the ratio GFR/RPF) is very similar to that found in normal pregnancy. Since previous work by the authors has shown that the normal pregnant patient has a reduced filtration rate and plasma flow, they suggest that all pregnant women are candidates for toxaemia but they do not suggest any trigger mechanism which might precipitate the disease. *D. C. A. Bevis*

235. **The Effect of Benzydroflumethiazide on Oedema of Pregnancy.**

By P. HOLCOMB. *Obstet. and Gynec.*, **17,** 455–459. Apr. 1961. 12 refs.

Benzydroflumethiazide is an orally active, non-mercurial, highly potent diuretic which differs from chlorothiazide by the addition of a benzyl and a trifluoro group to the parent molecule. It was found to be very effective when given to 50 pregnant patients with oedema in nearly all cases. The most effective dose was 5 mg. twice a day. *J. G. Dumoulin*

236. **The Use of Norethynodrel in Certain Reproductive Problems.**

By A. F. GOLDFARB and D. G. GONGSAKDI. *West. J. Surg. Obstet. Gynec.*, **69,** 92–95. Mar.–Apr. 1961. 10 refs. 8 tables.

The authors, from the Jefferson Medical College, review 77 patients with threatened and recurrent abortions who were treated with norethynodrel 10 mg. daily until the 16th week and then 20 mg. daily until the 32nd week of pregnancy. Extensive biochemical investigations were carried out and the result was that 79 per cent of the

repeated abortions and 60 per cent of the habitual abortions were salvaged. Four patients with repeated premature labours were successfully treated using the same dosage of the drug.

[These results are very similar to my own series of cases (Bevis (1951), *Lancet*, **2**, 207) in which no medication was used but similar biochemical investigations undertaken. It would appear that the "mumbo-jumbo" is more important than the pill or potion.]

*D. C. A. Bevis*

237. **Methemoglobinemia—A Cause of Abortions?**

By J. T. SCHMITZ. *Obstet. and Gynec.*, **17**, 413–415. Apr. 1961. 12 refs.

Methaemoglobinaemia is a cause of abortion in cattle in which it may be due to ingestion of forage high in nitrates.

The author examined methaemoglobin levels in 25 pregnant women. In 13 cases the pregnancy seemed normal and the mean level was 0·38 g. per 100 ml. In 9 cases threatening to abort it was 0·56 and in 3 who aborted 0·58. Thus, there seems to be a relationship between high maternal methaemoglobin levels and abortion.

Certain drugs can convert haemoglobin to methaemoglobin, principally phenacetin, nitrates, nitrites and aniline derivatives. Nitrites are common food preservatives and are generally present in sausage meats.

*J. G. Dumoulin*

238. **Septic Abortion with Vascular Collapse.**

By G. V. ANDERSON and M. KADNER. *West. J. Surg. Obstet. Gynec.*, **69**, 129–131. Mar.–Apr. 1961. 10 refs.

In an effort to reduce the mortality from septic abortion in Los Angeles County Hospital (1 in 323 abortions) the authors have instituted treatment with immediate infusion of 1 g. chloramphenicol in 200 ml. of intravenous fluid followed by 4–6 g. per 24 hours. Adequate blood or plasma transfusion is given and immediate evacuation of the uterus carried out, especially in the presence of hypotension. If hypotension is present, 200 mg. hydrocortisone are given intravenously and then 500 mg. are put in every litre of intravenous fluid to a total of 1,500 mg. in 24 hours. Vasopressors are used only if the urinary output decreases. Since using this regimen only 1 patient died out of 1,450 abortions.

*D. C. A. Bevis*

239. **Hypofibrinogenemia Associated with Placenta Previa and Placenta Previa Accreta.**

By S. H. CHERRY, K. ADAMSONS and L. L. PHILLIPS. *Surg. Gynec. Obstet.*, **112**, 551–558. May 1961. 2 tables. 5 figs. 21 refs.

Fifty cases of hypofibrinogenaemia occurred in the period 1956–1960 at the Sloane Hospital for Women, New York, among 20,000 deliveries, and the authors present 6 of these in whom the condition was associated with placenta praevia and placenta praevia accreta. The diagnosis of placenta praevia was made at the time of Caesarean section and the criteria for the diagnosis of placenta praevia accreta were the presence of villi within the myometrium and the absence of a decidua basalis.

This incidence of cases of hypofibrinogenaemia associated with placenta praevia is higher than in other reported series and it is suggested that this is due to the fact that blood coagulation studies are performed on all patients with significant bleeding and not merely in patients with a condition, such as abruptio placentae or amniotic fluid embolism, known to have associated clotting deficiency.

*A. E. R. Buckle*

240. **The Small Full-Term Infant and Placental Insufficiency.**

By W. L. RUMBOLZ, M. C. EDWARDS, and L. S. MCGOOGAN. *West. J. Surg. Obstet. Gynec.*, **69**, 53–60. Mar.–Apr. 1961. 10 tables. 28 refs.

The authors, from the University of Nebraska, review 57 babies delivered after the 36th week of pregnancy who weighed 2,050 g. or less. In all cases the growth of the uterus was much less than normal and this is taken as a warning sign of the condition. Twenty-three of the babies died (6 being abnormal) but those who survived rapidly attained a normal growth pattern and did not behave like "premature infants". In many cases the placenta was described as small and some of the others had numerous infarcts but it is pointed out that the placenta usually receives a most inadequate examination after delivery.

It is recommended that when the uterus fails to enlarge during the last trimester of pregnancy, the management of labour should in principle be that of a "premature" delivery, great attention should be paid to the development of foetal distress and little or no sedation should be used, delivery being carried out under conduction anaesthesia.

*D. C. A. Bevis*

241. **Cervical Incompetence.**

By L. BHOSE. *J. Obstet. Gynaec. India*, **11**, 315–322. Mar. 1961. 20 refs.

Two cases are described, and the literature is discussed.

*John McKiddie*

## LABOUR

242. **Isoxsuprine: A Myometrial Relaxant.**

By E. H. BISHOP and T. B. WONTERSZ. *Obstet. and Gynec.*, **17**, 442–446. Apr. 1961. 5 figs. 3 refs.

Isoxsuprine is a new compound of the phenethanolamine group which has a marked relaxant action on smooth muscle while producing minimal side-effects. When given by intravenous infusion in doses up to 500 μg./min., it was found to have little effect on the activity of the uterus in patients in spontaneous full term labour, whilst a larger dose produced hypotension and shock. However, the effect of the drug on cases of premature labour seemed to be the arrest of uterine contractions in a large percentage of cases.

*J. G. Dumoulin*

243. **Inflammation of the Placenta.**

By O. R. Emig, J. V. Napier and J. V. Brazil. *Obstet. and Gynec.*, **17**, 743–750. June 1961. 2 tables. 4 figs. 12 refs.

The placentae, membranes and cords from 709 deliveries showed microscopic evidence of inflammation in 13·3 per cent of cases. There was an increase in inflammatory reactions associated with rupture of the membranes for 12 hours or longer, and an increased incidence of prematurity and perinatal death in those showing evidence of inflammation. A clinical diagnosis of vaginal or cervical infection was made in half those cases showing inflammation of the placenta and membranes and in 20 per cent of a control group suggesting that more thorough attention should be paid to prenatal treatment of vaginitis and cervicitis. *J. G. Dumoulin*

244. **Prolapse of the Umbilical Cord.**

By N. K. Ghose and K. R. Dey. *J. Obstet. Gynaec. India*, **11**, 268–279. Mar. 1961. 11 refs.

One hundred and eleven cases occurring in the five-year period 1955–1959 were analyzed. The overall foetal mortality was 70 per cent. *John McKiddie*

245. **Conjoined Twins (Thoracopagus).**

By T. P. Shah. *J. Obstet. Gynaec. India*, **11**, 197–200. 1960. 1 fig. 5 refs.

A case history is given of conjoined twins delivered vaginally. Difficulty was experienced in delivering the first head which was delayed on the perineum. As there was no further advance, diagnosis was made by passing a hand along the ventral aspect of the foetus, and intra-uterine separation was carried out before further progress could be made and delivery achieved.

It is suggested that the possibility of such an abnormality should cross one's mind on looking at X-rays of all twins. The four criteria usually given for antenatal diagnosis are, that both heads should be at the same level and plane, that there is unusual backward flexion of both spines, that there is unusual proximity of the spines, and that there is no change in the relative positions after foetal movement, manipulation, or time. All of these criteria were absent in this case, X-ray showing one foetus lying vertically, the other transversely.

The combined weight of the twins was 10 pounds 6 ounces. Synchronous delivery in parallel was not practicable in this case as the twins were not presenting as breeches. Caesarean section was not considered as the diagnosis was made so late. It is advocated only if vaginal delivery fails. *John McKiddie*

## MATERNAL MORBIDITY

246. **The Incidence of Abortions in the Socialist Countries of Europe.** (Die Abortussituation in den europäischen sozialistischen Ländern.)

By K.-H. Mehlan. *Zbl. Gynäk.*, **83**, 853–866. June 3, 1961. 9 tables. 1 fig.

During the last decade abortion was legalized and social indications for termination of pregnancy were recognized in the U.S.S.R., Bulgaria, Hungary, Poland, Czechoslovakia and Yugoslavia, and temporarily in East Germany. Indications for termination were extended considerably in Sweden, Denmark, Japan and India. In the Soviet Union, Bulgaria and Hungary, there is no restriction whatever limiting abortions. All social grounds are accepted unconditionally and the decision is left entirely to the pregnant woman as to whether she wants to continue with the pregnancy or not, provided gestation has not exceeded 3 months.

In Czechoslovakia permission for termination is granted if a woman considers herself too old for having another child; if she has had many children; if her husband has died or is an invalid; if the family has broken up; if the woman is the main breadwinner in the family; and if, in the case of an unmarried woman, a difficult situation has arisen.

In the Soviet Union, Hungary and Yugoslavia, permission to terminate a pregnancy is granted by a committee which initially instructs the expectant mother that termination carries definite risks to life and health and may later be followed by sterility, that the social legislation makes provision for the needy, and that every abortion means the loss of a citizen to the community. If, in spite of such instruction, the woman remains unwilling to continue the pregnancy, interruption is sanctioned, provided there is no contra-indication.

An international symposium on the subject of abortion was held in Rostock in May, 1960, attended by experts from 17 countries. From the various reports it appeared that new legislation resulted in a very marked increase in the incidence of legal abortion. Thus, in Hungary, it rose from 2 per 10,000 inhabitants per year in 1952 to 123 in 1957 and 152 in 1959. This does not include criminal and other types of abortion. The absolute figures for the year 1959 were 267,000 abortions compared with 151,000 births. The reason why legalization of abortion did not completely do away with criminal abortion is attributed to a proportion of single and divorced women wishing to hide the pregnancy. However, over two-thirds of the applicants for abortion had more than 2 children.

Similar trends have been observed in Czechoslovakia. The ratio between abortions and births is about 1 : 1. There has been a marked reduction in the mortality following abortion from 63 in 1955 to 14 in 1959. One-third of the Czech women took the view that they should be free to decide on abortion without consulting their husband.

In Poland, where the Roman Catholic Church still has a fairly strong position, the incidence of legal abortion did not rise as steeply as in the other East European countries. The rate in 1958 was 15 per 10,000 head of population and rose to 27 in 1959. In 1960 the comparative figures for various East European countries were as follows: Hungary, 152; Czechoslovakia, 60; Bulgaria, 58; Yugoslavia, 50; Poland, 51; East Germany, 0·5.

Mehlan found that legalization of termination of

pregnancy did not reduce significantly the incidence of criminal abortion. He concluded that legalization was an unsuccessful method of reducing criminal abortion in Russia and East Germany, but in Czechoslovakia, Bulgaria, Poland and Hungary it led to a marked increase in legal abortions and decrease in criminal abortion and to a fall in the birthrate. The mortality rate of legal abortion averages 6 per 100,000 cases. The primary morbidity rate in 67,000 terminations between 1948 and 1951 was 3·6 per cent. Secondary infertility occurred in 2 per cent of cases investigated. Ten per cent of the women regretted the termination on social grounds for various reasons.

*Bruce Eton*

247. **Puerperal Tetanus.**

By J. C. PATEL, B. C. MEHTA, M. K. DHIRWANI and S. D. BHANDARKAR. *J. Obstet. Gynaec. India*, **11**, 187–192. 1960. 5 tables. 7 refs.

In India a domiciliary confinement frequently means that the patient is nursed on the floor which is made up of manure and straw, the midwife may be untrained, and dirty rags are used as vulval pads. Over a 4-year period 2,007 cases of tetanus were admitted to King Edward Memorial Hospital, Bombay, including 67 cases in the puerperium. Forty-five cases followed abortion, of which 34 died. Twenty-two cases followed vaginal delivery, of which 10 died. In the previous 11-year period there had been only 115 cases of puerperal tetanus in the same hospital, and the condition may be becoming more common.

*John McKiddie*

## ANAESTHESIA

248. **The Use of Drugs in Labour.** (Zur Frage der medikamentösen Geburtserleichterung.)

By H. VORHERR, G. STRAUSS and V. FRIEDBERG. *Geburts. u. Frauenheilk.*, **21**, 548–554. June 1961. 1 table. 2 figs. 39 refs.

A double blind trial was carried out on 337 patients to establish the effects of 50 mg. pethidine, 50 mg. *Monzal* (3,4-dimethoxy-phenyl-1-dimethyl-amino-4-phenyl-butane hydrochloride), *Efosin* (a mixture of 10 mg. diphenyl-piperidino-propane hydrochloride with 0·25 mg. diphenyl-piperidino-ethyl-acetamide hydrochloride), and 50 mg. *Erantin* (4-dimethyl-amino-1,2-diphenyl-3-methyl-2-propionyl-oxybutane) on the duration of normal labour, the frequency and duration of contractions (as recorded on Schwalm's partogramme), and the amount of pain experienced by the patients. The effects of these drugs were compared with a control group of patients given physiological saline. The first injection was given when the cervix was 2–3 cm. dilated and there were regular uterine contractions. A second and third injection of the same drug in the same dose was given at intervals of 1½ hours later. The only significant difference noted between the effects of the various drugs and the placebo was that pethidine had a greater analgesic effect.

*Peter J. Huntingford*

249. **Analgesia During Labour: A Comparison of Pentobarbital, Meperidine and Morphine.**

By C. CAMPBELL, O. C. PHILLIPS and T. M. FRAZIER. *Obstet. and Gynec.*, **17**, 714–718. June 1961. 6 tables. 5 refs.

A study was made of 212 term patients during labour, 71 of whom were given pentobarbital, 69 meperidine and 72 morphine for analgesia.

Ninety-six per cent of the meperidine-treated group, 89 per cent of the pentobarbital-treated group and 83 per cent of the morphine-treated group were satisfied with the treatment. Amnesia was successful in 54 per cent of the pentobarbital patients, 24 per cent of the morphine group and 23 per cent of the meperidine group; on the other hand more patients were unmanageable in the pentobarbital group than the others. There was little difference in the infants' results, as judged by a modified Apgar score 1 minute after birth.

*J. G. Dumoulin*

250. **Fluoromar Anesthesia in Obstetrics.**

By R. J. CAVALLARO and W. H. L. DORNETTE. *Obstet. and Gynec.*, **17**, 447–452. Apr. 1961. 3 tables. 7 refs.

Although their experience in its use is limited to 67 cases, the authors write enthusiastically about Fluoromar in obstetrics. This is a new anaesthetic agent, a volatile liquid, trifluorethylvinyl. It produced rapid, pleasant induction of anaesthesia, the level of which could be quickly altered. It is a potent analgesic also, non-toxic and stable, and it produces little depression of uterine contractility or of the foetus. There is some danger of over-dosage if too rapid an increase in concentration is given.

*J. G. Dumoulin*

## INFANT

251. **The Relation between Cortisone Therapy during Pregnancy and Congenital Malformations.** (Cortison, Schwangerschaft und Missbildungen des Neugeborenen.)

By H. LOHMEYER. *Geburtsh. u. Frauenheilk.*, **21**, 560–565. June 1961. 1 fig. 27 refs.

One hundred and twenty offspring of rats who were given 25–40 mg. of prednisone per 70 Kg. body weight daily by intramuscular injection before and during pregnancy were examined; in none of them was any congenital malformation found, although all of them showed hypoplasia of the adrenal cortex. Only 30 of the offspring survived 6 weeks, and in spite of substitution therapy with cortisone they remained about half the weight and size of the offspring in a control group.

The author also describes a woman of 27 who had been treated, because of eczema, for 2 years with 15–20 mg. of dexamethasone daily. The same treatment was continued throughout pregnancy. She delivered herself normally at term of a normal female infant weighing 2,150 g. The baby was not given cortisone after birth.

The author concludes that an association between cortisone therapy during pregnancy and congenital malformations of the infant is unlikely. However, growth

*in utero* may be retarded, and an increased neonatal morbidity and mortality may be expected, because of adrenocortical insufficiency. *Peter J. Huntingford*

252. **Umbilical Artery Aplasia.**

By W. A. LITTLE. *Obstet. and Gynec.*, **17**, 695–700. June 1961. 3 figs. 14 refs.

The umbilical cords from 1,200 placentae in 1958 disclosed 16 cases of single umbilical arteries, 4 of which were examples of 2 umbilical arteries fusing near the placental surface. There was no evidence of an increased incidence of pre-eclampsia but there was an association with velamentous insertion of the cord and placenta duplex.

This further report by the author includes 2,800 umbilical cord examinations in which 21 cases of aplasia of an umbilical artery were noted. Only 6 of the 21 cases were in primigravidae. Six of the 21 infants died prenatally and 1 postnatally, and 11 infants showed recognizable congenital abnormalities. *J. G. Dumoulin*

## GYNAECOLOGY

### DISORDERS OF FUNCTION

253. **The Pathological Normal Uterus.**

By R. D. DUNN. *West J. Surg. Obstet. Gynec.*, **69**, 178–181. May–June 1961. 2 figs. 5 refs.

By using the Weigert's-van Gieson staining technique, the author has found increased elastic tissue and collagen formation in the myometrium of uteri previously reported normal using the routine haematoxylin-eosin staining. He makes a plea for this examination of uteri removed for chronic pelvic symptoms in the absence of gross pathological change. *D. C. A. Bevis*

254. **The Artificial Vagina: Anatomic, Physiologic, Psychosexual Function.**

By W. H. MASTERS and V. E. JOHNSON. *West. J. Surg. Obstet. Gynec.*, **69**, 192–212. May-June 1961. 9 figs. 41 refs.

Three patients with artificial vaginae (2 McIndoe and 1 Frank) have been investigated in the Washington University Division of Reproductive Biology. Full sexual histories are given and it is stated that the artificial vagina goes through the same phases of excitement, plateau, orgasm and resolution as does the normal vagina. Cytological studies show that the vaginal skin has the normal menstrual phases in one patient who has ovaries while in another, without ovaries, the response to hormone administration is normal. The vaginal pH in all cases was within normal limits and the life of sperms within the tract was also normal.

[This is another part of a marathon investigation into sexual activity in the human animal conducted by the University of Washington. Previous reports are given in *West. J. Surg. Obstet. Gynec.*, 1960, **68**, 57; 1961, **69**, 105.] *D. C. A. Bevis*

255. **Medullary Resection of the Ovaries in Treatment of the Stein-Leventhal Syndrome.**

By H. KALLIO. *Acta obstet. gynec. scand.*, **40**, 16–25. 1961. 6 figs. 9 refs.

This is a report on 11 cases. In all the patients the periods became and remained regular; eight of the patients were married, and 5 of them became pregnant since the operation. *N. Alders*

### ENDOCRINOLOGY

256. **The Effect of Enavid, a Synthetic 19-Nor-steroid (Norethynodrel) on Post-menopausal Vaginal and Uterine Mucosa.**

By M. CRONQVIST and S. KULLANDER. *Acta obstet. gynec. scand.*, **40**, 43–58. 1961.

The effect of enavid on the endometrium and vaginal lining of post-menopausal women was studied by a double blind test on patients before they underwent operation for prolapse. Twenty-nine women were given enavid tablets (one tablet twice daily for 5 days), and 35 women were similarly given placebo tablets. Enavid produced proliferation, and in a few instances also secretion, of the endometrium, and a thick vaginal lining rich in glycogen. The patients' ages were between 40 and 79 years.

There was also slight activity of the endometrium and the vaginal lining in some of the women who had been given placebo tablets. This is ascribed to either stimulation by the curettage which always preceded the experiments, or to a low, rhythmical oestrogen production even in post-menopausal women.

[These findings would be more convincing if enavid tablets did not contain some oestrogens (ethinyl oestradiol-3-methyl ester).] *N. Alders*

257. **Induction of Ovulation in the Human with Human Gonadotrophins: Preliminary Report.**

By C. L. BUXTON and W. HERRMANN. *Amer. J. Obstet. Gynec.*, **81**, 584–590. Mar. 1961. 1 table. 6 figs. 7 refs.

For many years it has been apparent that species specificity is a major factor in pituitary ovarian relationships. In an attempt to meet this requirement in women the authors have used human pituitary gonadotrophin (HPG), got from human autopsy material regardless of age or sex of the subject, in the treatment of 7 patients who had either primary or secondary amenorrhoea for 3 to 6 years, and had received various forms of treatment without effect. They were now given a combination of human chorionic gonadotrophin (HCG) and HPG. Ten mg. of HPG were injected twice daily for 4 days followed by 10 mg. of HPG twice daily for 4 days, plus HCG 8,000 units twice daily. Five courses of therapy were given by this technique, all but two of which produced evidence of ovulation and menstruation. One woman who was menstruating normally but had endometriosis for which hysterectomy and removal of both ovaries became necessary, consented to undergo this combined therapy immediately before operation. Both ovaries were enlarged to 3 or 4 times normal size and

each contained several corpora lutea in different stages of development, which may have represented ovulations 24 to 36 hours apart.

In the 7 patients there were 2 failures. One was a case of congenital adrenal hyperplasia, and the other had had unsuccessful wedge resection of the ovaries for Stein Leventhal syndrome. It is impossible to say whether these ovulations were otherwise normal, but none of the patients became pregnant or continued to menstruate after therapy was stopped.

*F. J. Browne*

258. **The Effects of Anabolic Hormones on Vaginal Cytology.** (Zytologische Testung am Vaginalepithel von anabol wirksamen Hormonen.)

By W. WALZ. *Geburtsh. u. Frauenheilk.*, **21**, 455–471. May 1961. 7 tables. 11 figs. 14 refs.

The effects of Dianabol (methyl androstenolone) on the vaginal epithelium were observed. The smallest total dose that produced a recognizable effect was 75 mg.; this effect corresponded to that produced by about the same amount of testosterone propionate. The proliferation caused by Dianabol was, however, more intense. No further proliferation was observed after 75 mg. had been given, even with large doses in excess of this amount, or with small doses of 5 mg. daily given over a long period of time. The vaginal epithelium returned to its former state within 4–6 days of stopping the treatment. There was therefore no evidence of a cumulative effect. Oestrogenic proliferation was never seen, even with very large doses. In menopausal women a maximal artificially produced oestrogen proliferation could be suppressed with 50–75 mg. of Dianabol. The author concludes that in doses of up to 20 mg. daily Dianabol should have no effect on ovarian function, and that it may be used with safety in post-menopausal women.

*Peter J. Huntingford*

259. **Corticosteroids in the Treatment of Non-Patent Fallopian Tubes.**

By J. I. KURLAND and C. H. LOUGHRAN. *Amer. J. Obstet. Gynec.*, **81**, 243–249. Feb. 1961. 1 table. 9 figs. 11 refs.

Because of the anti-inflammatory properties of corticosteroids 20 cases of tubal occlusion were treated by them without addition of any antibiotics or other drugs. The occlusion was demonstrated in 5 of the 11 successful cases by 2 salpingograms, in 3 cases by Rubin tests plus one salpingogram, in 2 by one salpingogram plus indigocarmine, and in one case by one salpingogram. In most there was a history of pelvic inflammatory disease and post-abortal infection. The drug used was Cortogen (Schering) 50 mg. daily by tablet, plus 50 mg. intramuscularly twice weekly, or meticortelone acetate (Schering), 10 mg. daily by mouth plus 25 mg. intramuscularly twice weekly. Both were given for 3 to 6 months. Of the 20 cases 11 demonstrated tubal patency after 3 to 6 months' treatment and 6 of these became pregnant. There were no serious side-effects or toxic symptoms.

*F. J. Browne*

## INFECTIONS

260. **Investigations into the Symptomatology of Women Infected with Trichomonas.** (Untersuchungen zur Frage der Symptomatik der trichomonasinfizierten Frau.)

By J. HOLTORFF. *Zbl. Gynäk.*, **83**, 725–734. May 13, 1961. 4 tables. 26 refs.

The author studied 391 women with trichomonas infection and a control group of 234 healthy women, and gives a detailed report of the symptoms. He points out that a characteristic clinical picture of trichomonas vaginitis is rare. In only one-quarter of the infected cases are the manifestations obvious; one-quarter is completely symptom-free; in the majority of infected patients the symptoms are scanty and mild.

*Bruce Eton*

261. **The Oral Treatment of Trichomonas Vaginitis with Metronidazole.** (Die orale Behandlung der Trichomoniasis urogenitalis der Frau mit Metronidazol.)

By J. M. BEDOYA and J. M. FERNANDEZ-ORTEGA. *Geburtsh. u. Frauenheilk.*, **21**, 574–578. June 1961. 2 tables. 15 refs.

Seventeen out-patients and 17 in-patients with trichomonas vaginitis were given metronidazole 250 mg. orally twice a day for 7 days. The husbands of married women out-patients were given the same course of treatment. All of the patients were free from infection at the end of the course of treatment, and had remained so one month later.

*Peter J. Huntingford*

262. **The Treatment of Trichomoniasis in the Female with Metronidazole ("Flagyl"), A New Derivative of Imidazole, with Particular Reference to Infection of the Female Urethra and the Male Urogenital System.** (Traitement de la trichomoniase de la femme par le metronidazol, nouveau dérivé de l'imidazole en se référant particulièrement à l'infestation de l'urèthre feminin et de l'appareil uro-génital chez l'homme.)

By P. LUNDSTROM and L. PETERSOHN. *Gynéc. prat.*, **12**, 171–183. 1961. 30 refs.

Forty patients were treated. Those in whom the flagellate was recovered only from the vagina received local treatment with one 0·5 g. pessary daily for twenty days. If trichomonads were also found in the urethra, this routine was supplemented by oral therapy consisting of 0·25 g. twice daily for ten days. Twenty-eight of the male consorts were examined. Only 3 were infected. They were treated orally. Two of the women with vaginal trichomoniasis only also received oral therapy as they "had had symptoms for a long time". No restrictions were placed on coital activity.

After this therapy there were 7 relapses. In none of these had the urethra been infected. These 7 women were re-treated with both local and oral therapy. Five of them were indulging in regular coitus and the male partner of each of these was treated orally. One of the 7 relapses failed to achieve a cure on her second course but positively denied intercourse.

On the strength of these observations the authors consider that the cure rate with this therapy is over 95

per cent and that urethral infection in both male and female play only minor roles in relapse.

There is an interesting incidental observation in that 30 per cent of 650 gynaecological patients seen in six months at the clinic in which the authors practice complained mainly or entirely of a vaginal discharge.

*Geoffrey Dixon*

263. **Actinomycosis of the Female Genital Tract.** (Aktinomykose der weiblichen Genitalien.)

By K. Breyer. *Zbl. Gynäk.*, **83**, 738–743. May 13, 1961. 12 refs.

After reviewing the literature on the subject, the author reports two cases of actinomycosis, The first case occurred in a 19-year-old parous farmer's wife whose initial complaint was pain in the vagina and rectum during coitus. She had been using leaves after defaecation for many years. Multiple fistulae developed and discharged pus into the rectum and from the vulva. A swelling formed in the vagina which increased to the size of a hen's egg. There was a nodule in the left groin, adherent to the skin. The vaginal swelling was excised and histological examination established the diagnosis. No lesions were found elsewhere.

The second case was that of a single parous woman. She had induced an abortion one year previously by means of a marsh-mallow root. Her periods subsequently became irregular and prolonged. She complained of pelvic pain and clinical examination revealed a fixed slightly tender mass on the left side of the uterus, the size of a small apple. X-ray examination did not show any pulmonary lesions. Laparotomy revealed thickening and enlargement of both Fallopian tubes and a right tubo-ovarian mass which was adherent to the surrounding tissues. The tubes and right ovarian mass were excised. Histological examination showed that the infection was due to actinomycosis.

Treatment in both cases was begun with penicillin and sulphonamide, without success. After the operation Terramycin and "Geomycin" were administered with excellent results. The total duration of this treatment amounted to three weeks.

*Bruce Eton*

## NEW GROWTHS

264. **Precursors of Corpus Cancer.**

By S. B. Gusberg and R. E. Hall. *Obstet. and Gynec.*, **17**, 397–412. Apr. 1961. 22 figs. 6 refs.

This is a study of 23 patients with endometrial cancer arising after prolonged continuous oestrogen administration. Each had been taking oestrogens for 1–20 years, although not necessarily in large amounts. The common histological finding when the endometrium was examined was adenomatous hyperplasia with malignant properties in which the cancer was papillary and well differentiated, suggesting that there is a relationship between unopposed oestrogen stimulation and endometrial cancer.

*J. G. Dumoulin*

265. **The Colpomicroscope in the Diagnosis of Benign and Pre-malignant Lesions of the Cervix Uteri.**

By Ting-chao Wong, J. H. Austin, P. A. Younge and D. G. McKay. *Obstet. and Gynec.*, **17**, 665–673. June 1961. 3 tables. 5 figs. 28 refs.

The authors report on the use of this instrument in inspecting 100 abnormal cervices. The cervix is first cleaned and then rapidly stained with 1 per cent toluidine blue. There was a high degree of accuracy in diagnosing 17 cases of anaplasia or carcinoma *in situ* and 83 benign lesions when compared with other cytological and histological methods. The microscope method only reveals lesions of the portio and will not detect endocervical canal lesions, otherwise it appears to be as useful as a biopsy method.

*J. G. Dumoulin*

266. **On the Use of Cresyl Violet as a Stain in Colpocytology.** (Sull'uso del cresil violetto come colorante in colpocitologia.)

By C. Pasquinucci. *Ann. Ostet. Ginec.*, **83**, 472. May 1961. 8 figs. 7 refs.

The author describes a method for staining vaginal smears, using Cresyl Violet. He has found this most useful in the diagnosis of malignancy as the nuclei are very perfectly stained. The method is less useful for the diagnosis of functional conditions as it does not show up the general cellular characteristics as well as other methods of staining.

*Josephine Barnes*

267. **Critical Points of Failure in the Therapy of Cancer of the Cervix: A Study of 250 Recurrences.**

By E. W. Munnell and W. A. Bonney. *Amer. J. Obstet. Gynec.*, **81**, 521–534. Mar. 1961. 9 tables. 14 figs. 14 refs.

This is an account of all the recurrences seen after treatment of cancer of the cervix at the Sloane Hospital for Women and the Francis Delafield Hospital, New York, from 1940 to 1957.

The most common sites of recurrence were (*a*) "central pelvic" (17 per cent of cases), where the recurrence was thought to be limited to the cervix and vaginal vault, and (*b*) "deep pelvic" (60 per cent of cases) where the recurrence was believed to involve the lateral parametrium and utero-sacral ligaments and the iliac, hypogastric or obturator lymph nodes. These figures suggest that the weak spot both in radiation therapy of the primary disease and in radical surgical excision is at the periphery of the disease, and that each modality fails most frequently to destroy or remove all the malignant cells in these deep pelvic tissues.

Most patients were not aware that a recurrence was present and it was only detected by pelvic examination. The first sign was usually pain, generally in the lower back, hip or pelvis, with or without radiation down the leg. Obstructive uropathy was the first symptom in 10 per cent, but when intravenous pyelography was done it showed ureteric obstruction in 90 per cent, usually close to the bladder. Sixty per cent of the recurrences were first evident within 1 year after therapy, and by 2½ years

85 to 90 per cent had appeared. There were 17 recurrences that did not appear till long after 5 years had passed. All these had been treated by radiation.

The value of treatment of recurrence is sharply limited. Central pelvic recurrences should be treated not only to prolong survival time but possibly also to achieve an occasional cure. The same may be said of deep pelvic recurrences but not so strongly. When bladder and rectum were involved the best that treatment offered was slight prolongation of survival time, and when pelvic bone, inguinal nodes, extra-pelvic nodes or distant organs became involved treatment was of no value. Of the 250 patients who had recurrence only 5 were salvaged. Management of recurrence is rendered more difficult by the fact that clinical diagnosis of the extent of spread is usually highly inaccurate and over optimistic.

Patients with central pelvic recurrence after primary radiotherapy seem to be best treated by radical hysterectomy, though sometimes repeat radiation may be preferable. Those with recurrence following primary operation are usually best treated by radiation.

The authors' results with exenteration have been unsatisfactory and there have been no 5-year survivors. It is suggested that recurrence might be diagnosed much earlier by intravenous pyelography and that this should be done at least every 6 months for the first 2½ years after completion of primary therapy. Any abnormality in the pyelogram should create suspicion of recurrence.

*F. J. Browne*

268. **Adenocarcinoma of the Cervix.** (Carcinoma cilindrico del cuello del útero.)

By N. ARENAS. *Obstet. Ginec. lat. amer.*, **17**, 415–417. 1959. 3 microphotographs. 6 refs.

The author gives detailed report of 5 cases of adenocarcinoma of the cervix which he found in a survey of 106 patients suffering from carcinoma of the cervix.

*John F. Foulkes*

269. **The Amazing Granulosa Cell Tumour.**

By L. G. BALDWIN. *West. J. Surg. Obstet. Gynec.*, **69**, 89–91. Mar.–Apr. 1961. 17 refs.

The author reviews the literature and concludes that a few of these tumours are highly malignant but that most can be treated conservatively if carcinoma of the body of the uterus is excluded. They can produce a positive biological test of pregnancy and can also produce masculinization. Recurrences are common and radiotherapy is of questionable value.

*D. C. A. Bevis*

270. **Meigs' Syndrome Due to Struma Ovarii.** (Meigs' Syndrom und struma ovarii.)

By K. E. ZELLNER. *Acta obstet. gynec. scand.*, **40**, 40–42. 1961. 7 refs.

This is short description of a Meigs's syndrome caused by a struma ovarii.

*N. Alders*

## GYNAECOLOGICAL OPERATIONS

271. **Is Pregnancy Still Possible After Obligatory Bilateral Salpingo-oöphorectomy?** (Peut-on encore espérer une grossesse après l'extirpation obligatoire des trompes et des ovaires?)

By C. STANCA, M. V. JONESCO and A. POPA. *Gynéc. prat.*, **12**, 161–169. 1961. 1 fig. 7 refs.

It is sometimes necessary to remove both tubes from a patient who still desires a pregnancy. The authors discourse briefly on the functions of the Fallopian tube and conclude that the only requisites for female fertility are an intact uterus and some small portion of ovarian tissue in that organ.

They believe that most ovarian grafts into the cavity of the uterus fail because more or less intact ovaries are left in their normal situation. They maintain that in this circumstance all pituitary stimulation falls on the normally situated ovaries and that the grafted tissue is "deprived of all hormonal stimulation", and will therefore atrophy.

If, however, both ovaries are removed at the time of the salpingectomy and a free graft of a slice of ovarian tissue is made into the uterine cavity, without any pedicle, they believe that the pituitary action will be concentrated on the graft alone and thus "stimulate and revitalize it".

The authors illustrate the article with one detailed case report and claim a total of three pregnancies from "a considerable number of operations". Both the other pregnancies ended in abortion.

*Geoffrey Dixon*

272. **Urinary Diversion in Pelvic Exenteration.**

By J. J. MURPHY and J. J. MIKUTA. *Surg. Gynec. Obstet.*, **112**, 743–747. June 1961. 2 tables. 5 figs. 13 refs.

Experience gained with isolated bowel conduits for urinary diversion in 74 patients (26 with pelvic exenteration, 23 in persons with "useless bladders", 13 with cystectomy, 9 with intractable vesico-vaginal fistulas and 3 for palliative reasons) are discussed.

Either isolated ileal or sigmoid colon conduits were employed and, after a description of the operative technique employed, the authors describe the follow-up evaluation of renal status. Sixty-nine patients have been followed up for more than a year, 18 showing improvement, 44 showing no change and 7 being worse. Electrolyte imbalance has not been found to be a problem in these patients.

It is concluded that, as successful eradication of cancer may be nullified by complications associated with diversion of urine, the use of isolated bowel conduits, with their lessened risk, should provide for an honest evaluation of pelvic exenteration.

*A. E. R. Buckle*

273. **Reconstruction of a Functioning Vagina Following Radiation Therapy for Cancer of Cervix.**

By R. J. SIMMONS and D. R. MILLARD, JR. *Surg. Gynec. Obstet.*, **112**, 761–762. June 1961. 6 refs.

The authors describe a method of forming a new vaginal pocket by dissection between the posterior vaginal wall and the rectum. A skin graft on a suitable mould is introduced to line the cavity. *A. E. R. Buckle*

274. **Transabdominal Repair of Cystocele.**
By G. A. MACER. *West. J. Surg. Obstet. Gynec.*, **69**, 182–184. May–June 1961. 3 figs. 6 refs.

The author, from the University of Southern California, advocates this operation solely for the correction of cystocele in patients who must undergo laparotomy; it should be reserved for small to moderate cystoceles and is not intended to replace the usual methods of vaginal surgery. Total abdominal hysterectomy is performed in the usual manner except that before cutting the vagina, the bladder is mobilized by gauze dissection until the ureteral bundles can be palpated as they enter the bladder. It is advisable to stay close to the midline or the vesical plexus may give trouble, but bleeding can be controlled by pressure. The pubo-cervico-vesical fascia is mobilized by a transverse incision over the cervix and is then incised along the axis of the vagina. The uterus is removed and an ellipse of vaginal mucosa excised, the major axis being at the line of greatest relaxation. The edges of the vagina are now approximated by a continuous suture and a second row of sutures placed in the pubo-cervico-vesical fascia to support the floor of the bladder. The vaginal vault is now closed, but additional support can be obtained by including the cut edges of the cardinal ligaments and by plicating the utero-sacral ligaments with non-absorbable sutures. If a urethrocele is present, a Kelly type of repair is done *per vaginam* and a posterior repair performed for further support.

Fifty-five patients have been treated in ten years and the results are regarded as favourable.

*D. C. A. Bevis*

## UROLOGY

275. **A New Apparatus for Cystometry and Sphincterometry in Gynaecology.** (Die Zystometrie und Sphinkterometrie in der Gynäkologie mit neuen Geräten.)
By L. BECK. *Geburtsh. u. Frauenheilk.*, **21**, 444–454. May 1961. 7 figs. 21 refs.

The author has designed an apparatus that enables the bladder tone to be measured continuously whilst it is being filled at constant pressure and temperature. With the same apparatus it is also possible to measure the strength of the vesical sphincter before and whilst fluid is flowing through the urethra.

The vesical sphincter usually opens with a pressure of 50–65 mm. Hg. The normal sphincter remains competent as long as the pressure required to open it is above 50 mm. Hg. Voluntary contraction of the pelvic floor normally produces a further increase of pressure in the order of 10–20 mm. Hg. In a normal bladder the pressure, whilst it is being filled, varies between 10 and 15 mm. Hg; the pressure increases by about 1·5 mm. Hg per 100 ml. of fluid. At the onset of micturition the pressure suddenly rises to 50–60 mm. Hg, and even higher if the intra-abdominal pressure is voluntarily increased. The first desire to micturate is usually felt when the bladder contains 200–300 ml.; a painful urge is felt with 400–600 ml. Urge incontinence is present if the first desire to micturate is felt with volumes less than 150 ml., and if a definite rise in pressure occurs when the bladder contains 200–250 ml.

This apparatus is simple to use, and suitable for clinical practice. It gives valuable information in the following conditions: cases of stress incontinence without prolapse; persistent stress incontinence after repair operations; the differential diagnosis of urge and stress incontinence; and as a research tool for the exact assessment of pre- and post-operative urinary symptoms.

*Peter J. Huntingford*

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# ROYAL COLLEGE OF OBSTETRICIANS AND GYNAECOLOGISTS

AT the meeting of Council held in the College on Saturday, 23rd September, 1961, with the President, Mr. A. C. H. Bell, in the Chair, the following were admitted to the **Fellowship:**

David Robinson Cairns

Matthew Henry Vincent Young

The following were admitted to the **Membership:**

Frederick Douglas Adey
Farid Akasheh
James Harvey Andrew
Mukundadas Auddy
Amy Pushpam Augustus
Carmino Antonio Barbaro
Subodh Chandra Basak
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